

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 FEB 25 CA/CAPLUS - Russian Agency for Patents and Trademarks
(ROSPATENT) added to list of core patent offices cove
NEWS 4 FEB 28 PATDPAFULL - New display fields provide for legal sta
data from INPADOC
NEWS 5 FEB 28 BABS - Current-awareness alerts (SDIs) available
NEWS 6 FEB 28 MEDLINE/LMEDLINE reloaded
NEWS 7 MAR 02 GBFULL: New full-text patent database on STN
NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS 9 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 10 MAR 22 KOREAPAT now updated monthly; patent information enha
NEWS 11 MAR 22 Original IDE display format returns to REGISTRY/ZREGI
NEWS 12 MAR 22 PATDPASPC - New patent database available
NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental propert

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

All use of STN is subject to the provisions of the STN Customer
agreement. Please note that this agreement limits use to scientific
research. Use for software development or design or implementation
of commercial gateways or other similar uses is prohibited and may
result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 07:59:12 ON 04 APR 2005

=> file uspatful

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION

FULL ESTIMATED COST

0.21 0.21

FILE 'USPATFULL' ENTERED AT 07:59:21 ON 04 APR 2005

CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 31 Mar 2005 (20050331/PD)
FILE LAST UPDATED: 31 Mar 2005 (20050331/ED)
HIGHEST GRANTED PATENT NUMBER: US6874161
HIGHEST APPLICATION PUBLICATION NUMBER: US2005071904
CA INDEXING IS CURRENT THROUGH 31 Mar 2005 (20050331/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 31 Mar 2005 (20050331/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2005

>>> USPAT2 is now available. USPATFULL contains full text of the
>>> original, i.e., the earliest published granted patents or
>>> applications. USPAT2 contains full text of the latest US
>>> publications, starting in 2001, for the inventions covered in
>>> USPATFULL. A USPATFULL record contains not only the original
>>> published document but also a list of any subsequent
>>> publications. The publication number, patent kind code, and
>>> publication date for all the US publications for an invention
>>> are displayed in the PI (Patent Information) field of USPATFULL
>>> records and may be searched in standard search fields, e.g., /PN,
>>> /PK, etc.

>>> USPATFULL and USPAT2 can be accessed and searched together
>>> through the new cluster USPATALL. Type FILE USPATALL to
>>> enter this cluster.
>>>
>>> Use USPATALL when searching terms such as patent assignees,
>>> classifications, or claims, that may potentially change from
>>> the earliest to the latest publication.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s us4808536/pn
L1 1 US4808536/PN

=> d l1,cbib,ab,clm

L1 ANSWER 1 OF 1 USPATFULL on STN
89:14999 Immunochemical method for detection of antibody against HTLV-
protein based upon recombinant HTLV-III gag gene encoded protein.
Chang, Nancy T., Houston, TX, United States
Ghrayeb, John, Thorndale, PA, United States
Centocor, Inc., Malvern, PA, United States (U.S. corporation)
US 4808536 19890228 <-
APPLICATION: US 1986-834212 19860227 (6)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Immunochemical assays for detection of antibodies against HTLV-
proteins are described. The assays are based upon recombinant HT

core proteins expressed by cloned DNA segments of the gag region HTLV-III genome. Immunoreactive, chimeric HTLV-III core protein methods of producing these proteins are also described.

CLM

What is claimed is:

1. A method of detecting antibody against HTLV-III core protein biological fluid, comprising the steps of: a. providing an antigen immunoadsorbent comprising a solid phase to which is attached a core antigen which is a chimeric antigen comprising an amino acid sequence beginning at amino acid number 1 through 99, and extending to amino acid number 228, as shown in FIG. 5, the chimeric antigen immunoreactive with antibody against HTLV-III core protein; b. incubating the immunoadsorbent with a sample of the biological fluid to be tested under conditions which allow antibody in the sample to react with the antigen immunoadsorbent; c. separating the immunoadsorbent from the sample; and d. determining antibody bound to the immunoadsorbent as an indication of antibody against HTLV-III core protein in the sample.

2. A method of claim 1, wherein the HTLV-III antigen is the pG2 polypeptide having an amino acid sequence substantially as shown in FIG. 5.

3. A method of claim 1, wherein the biological fluid is human serum or plasma.

4. A method of claim 1, wherein the step of determining the antibody bound to the immunoadsorbent comprises: (a) incubating the immunoadsorbent with a labeled antibody against immunoglobulin of a species from which the biological fluid is derived; (b) separating the immunoadsorbent from the labeled antibody; and (c) detecting the label associated with the immunoadsorbent as an indication of antibody against HTLV-III core protein in the sample.

5. A method of claim 4, wherein the biological fluid is human plasma or serum, and the labeled antibody is labeled anti-human IgG antibody.

6. A method of detecting antibody against HTLV-III core protein in plasma or serum, comprising the steps of: (a) providing an antigen immunoadsorbent comprising a polystyrene bead coated with an essentially homogeneous preparation of pG2 polypeptide having the amino acid sequence substantially as shown in FIG. 5; (b) incubating the immunoadsorbent with a sample of human plasma or serum under conditions which permit anti-HTLV-III core protein antibody in the sample to form a complex with the pG2 polypeptide; (c) separating the immunoadsorbent from the sample; (d) incubating the immunoadsorbent with a solution of labeled anti-human Ig antibody; (e) separating the immunoadsorbent from the solution of labeled antibody; and (f) detecting the label associated with the immunoadsorbent as an indication of anti-HTLV-III core protein antibody in the sample.

7. An immunoadsorbent comprising a solid phase support having at

thereto a HTLV-III core protein which is a chimeric antigen, comprising an amino acid sequence beginning at amino acid number 1 through 99 and extending to amino acid number 228, as shown in FIG. 5, the chimeric antigen being immunoreactive with antibody against HTLV-III core protein.

8. An immunoabsorbent of claim 7, wherein the recombinant HTLV-III protein is pG2 polypeptide having the amino acid sequence substantially as shown in FIG. 5.

9. An assay for antibody against HTLV-III in a biological fluid comprising the steps of: a. providing an immunoabsorbent comprising a solid phase to which is attached a mixture of (i) HTLV-III core protein which is a chimeric antigen, comprising an amino acid sequence beginning at amino acid number 1 through 99, and extending to amino acid number 228, as shown in FIG. 5, the chimeric antigen being immunoreactive with antibody against HTLV-III envelope protein immunoreactive with antibody against HTLV-III envelope protein; (b) incubating the immunoabsorbent with a sample of biological fluid; (c) separating the immunoabsorbent from the sample; and (d) determining antibody bound to the immunoabsorbent as an indication of antibody against HTLV-III in the sample.

10. An assay for antibody against HTLV-III in a biological fluid comprising the steps of: (a) providing an immunoabsorbent comprising a solid phase to which is attached approximately an equal amount of pG2 polypeptide having the amino acid sequence substantially as shown in FIG. 5 and HTLV-III polypeptide 121; (b) incubating the immunoabsorbent with a sample of biological fluid; (c) separating the immunoabsorbent from the sample; and (d) incubating the immunoabsorbent with a sample of anti-human Ig antibody; (e) separating the immunoabsorbent from the sample; (f) detecting the label associated with the immunoabsorbent as an indication of anti-HTLV-III antibody in the sample.

11. An immunoabsorbent comprising a solid phase coated with an essentially equal amount of pG2 polypeptide having an amino acid sequence substantially as shown in FIG. 5 and polypeptide 121.

12. A HTLV-III core antigen immunoreactive with antibody against HTLV-III core protein the antigen comprising an amino acid sequence beginning at amino acid number 1 through 99, and extending to amino acid number 228, as shown in FIG. 5.

13. pG2 polypeptide having the amino acid sequence substantially as shown in FIG. 5.

14. An essentially homogeneous preparation of pG2 of claim 13 which is 98% pure protein.

15. A method of detecting antibody against HTLV-III core protein

biological fluid, comprising the steps of: (a) providing an anti immunoadsorbent comprising a solid phase to which is attached an HTLV-III core antigen immunoreactive with antibody against HTLV protein, the HTLV-III core antigen comprising an amino acid sequence beginning at amino acid number 1 through 99, and extending to amino acid number 228, as shown in FIG. 5; (b) incubating the immunoadsorbed sample of the biological fluid to be tested under conditions which allow antibody in the sample to complex with the antigen immunoadsorbent; (c) separating the immunoadsorbent from the sample; (d) determining antibody bound to the immunoadsorbent as an indication of the antibody against HTLV-III core protein in the sample.

16. A kit for detecting antibody against HTLV-III core protein in biological fluids, comprising, in separate containers, the components: a. an immunoadsorbent coated with a HTLV-III core polypeptide with a chimeric antigen, comprising an amino acid sequence beginning at amino acid number 1 through 99, and extending to amino acid number 228 as shown in FIG. 5, the chimeric antigen being immunoreactive with antibody against HTLV-III core protein; and b. an anti-(human IgG) antibody.

17. A kit of claim 16, wherein the HTLV-III core protein has the amino acid sequence substantially as shown in FIG. 5.

18. A kit of claim 16, further comprising: (a) a diluent for the biological fluid; (b) a positive control solution; and (c) a negative control solution.

19. A kit of claim 18, wherein the positive control solution is containing antibody against polypeptide 121 and the negative control solution is sera that does not contain antibody against polypeptide 121.

20. A method of detecting antibody against HTLV-III core protein in biological fluid, comprising the steps of: a. providing an anti immunoadsorbent comprising a solid phase to which is attached a HTLV-III core antigen immunoreactive with antibody against HTLV protein, the chimeric antigen comprising an amino acid sequence beginning at amino acid number 1 through 99, and extending to amino acid number 228, as shown in FIG. 5; b. incubating the immunoadsorbed sample of the biological fluid to be tested under conditions which allow antibody in the sample to complex with the antigen immunoadsorbed; c. separating the immunoadsorbent from the sample; and d. determining antibody bound to the immunoadsorbent as an indication of antibody against HTLV-III core protein in the sample.

21. A method of claim 20, wherein the polypeptide is pG2 having the amino acid sequence substantially as shown in FIG. 5.

=> s us5001230/pn

L2 1 US5001230/PN

=> d 12,cbib,ab,clm

L2 ANSWER 1 OF 1 USPATFULL on STN

91:22742 T cell activation markers.

Brown, Keith D., Hunters Hill, Australia

Mosmann, Timothy K., Atherton, Canada

Zurawski, Gerard, Redwood City, CA, United States

Kurawski, Sandra M., Redwood City, CA, United States

Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
US 5001230 19910319 <-

APPLICATION: US 1988-157743 19880218 (7)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A polypeptide designated H400 and its encoding nucleic acid are as markers specific for activated human T cells. Activated t cel detected immunochemically by monoclonal antibodies specific for its immunogenic peptides. Activated T cells are also detected by acid probes directed to messenger RNA encoding the H400 protein.

CLM What is claimed is:

1. A nucleic acid capable of encoding the mature polypeptide of reading frame defined by the following amino acid sequence: ##ST

2. The nucleic acid of claim 1 defined by the following nucleotide sequence: ##STR5##

=> s us5874225/pn

L3 1 US5874225/PN

=> d 13,cbib,ab,clm

L3 ANSWER 1 OF 1 USPATFULL on STN

1999:24450 Identification of compounds that modulate HIV-1 vpr protein

Weiner, David B., Merion, PA, United States

Levy, David Nathan, Philadelphia, PA, United States

Trustees of The University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
The Wistar Institute, Philadelphia, PA, United States (U.S. corporation)

US 5874225 19990223 <-

APPLICATION: US 1993-19601 19930219 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed toward methods of identifying compounds which inhibit the human immunodeficiency virus (HIV) v protein R (Vpr) from stimulating the differentiation of undifferentiated cells. This invention takes advantage of the observation that ce

from rhabdomyosarcomas, which are tumors of muscle origin, have used as models of CD4-independent HIV infection. These cell line induced to differentiate in vitro. The vpr gene of HIV-1 is sufficient for the differentiation of the human rhabdomyosarcoma cell line. Differentiated cells are characterized by great enlargement, altered morphology, lack of replication, and high level expression of the muscle-specific protein myosin. Morphological differentiation and inhibition of proliferation of other transformed cell lines follow vpr expression was also observed. This invention also relates to methods of identifying compounds which inhibit HIV Vpr binding to these cells. These screening methods should facilitate the identification and development of antiviral agents.

CLM

What is claimed is:

1. An in vitro method of identifying compounds that are capable of inhibiting HIV-1 Vpr-mediated differentiation of undifferentiated cells comprising the following steps: (I) contacting undifferentiated cells with HIV-1 Vpr in the presence or absence of a test compound; and (II) determining whether said cells cease proliferating and display cellular differentiation markers in the presence or absence of a test compound wherein the presence of cellular proliferation and absence of differentiation markers in the test sample is indicative of said compound being capable of inhibiting HIV-1 Vpr-mediated differentiation of undifferentiated cells.

2. The method of claim 1 wherein said undifferentiated cells are selected from the group consisting of: solid muscle tumor alveolar rhabdomyosarcoma cell line RD, solid muscle tumor alveolar rhabdomyosarcoma cell line TE671, osteosarcoma cell line D17, osteosarcoma cell line MG63, osteosarcoma cell line HOS-TE86, myeloid lineage cell line KG-1, myeloid lineage cell line THP-1, myeloid cell line PLB973, human glioblastoma cell line U-138MG, human glioblastoma/astrocytoma cell line U373MG, and human glioblastoma/astrocytoma cell line U87-MG.

3. An in vitro method of identifying compounds that are capable of inhibiting HIV-1 Vpr-mediated suppression of cellular proliferation comprising the following steps: (I) contacting proliferating cells with HIV-1 Vpr in the presence or absence of a test compound; and (II) determining whether said cells cease proliferating in the presence or absence of said test compound; wherein the presence of cellular proliferation in the test sample is indicative of said compound being capable of inhibiting HIV-1 Vpr-mediated suppression of cellular proliferation.

4. The method of claim 3 wherein said proliferating cells are selected from the group consisting of: solid muscle tumor alveolar rhabdomyosarcoma cell line RD, solid muscle tumor alveolar rhabdomyosarcoma cell line TE671, osteosarcoma cell line D17, osteosarcoma cell line MG63, osteosarcoma cell line HOS-TE86, myeloid lineage cell line KG-1, myeloid lineage cell line THP-1, myeloid

cell line PLB973, human glioblastoma cell line U-138MG, human glioblastoma/astrocytoma cell line U373MG, and human glioblastoma/astrocytoma cell line U87-MG.

5. An in vitro method for the identification of compounds capable of inhibiting HIV-1 Vpr binding to HIV-1 Gag comprising the following steps: (i) contacting, in the presence or absence of a test compound, HIV-1 Vpr and Gag; and (ii) determining the level of binding between HIV-1 Vpr and Gag, wherein a reduction in binding in the presence of a test compound is indicative of said compound being capable of inhibiting HIV-1 Vpr binding to Gag.

6. The method of claim 5 wherein said binding level is determined by the addition of a labeled antibody.

7. The method of claim 5 wherein said HIV-1 Vpr and Gag are from eukaryotic cells.

8. The method of claim 5 wherein said HIV-1 Vpr and Gag are from insect cells.

9. The method of claim 5 comprising the following steps: (i) contacting, in the presence or absence of a test compound, eukaryotically expressed HIV-1 Vpr and Gag, wherein said Vpr is attached to a solid support; (ii) washing the mixture of step (i) to remove unbound Gag protein; and (iii) determining the level of binding between HIV-1 Vpr and Gag through the addition of a Gag-specific labeled antibody, wherein a reduction in binding in the presence of the test compound is indicative of said compound being capable of inhibiting HIV-1 Vpr binding to Gag.

10. The method of claim 9 wherein said HIV-1 Vpr and Gag are from insect cells.

11. The method of claim 5 comprising the following steps: (i) contacting, in the presence or absence of a test compound, eukaryotically expressed HIV-1 Vpr and Gag, wherein said Gag is attached to a solid support; (ii) washing the mixture of step (i) to remove unbound Vpr protein; and, (iii) determining the level of binding between HIV-1 Vpr and Gag through the addition of a Vpr-specific labeled antibody, wherein a reduction in binding in the presence of the test compound is indicative of said compound being capable of inhibiting HIV-1 Vpr binding to Gag.

12. The method of claim 11 wherein said HIV-1 Vpr and Gag are from insect cells.

=> e weiner david b/in

E1 9 WEINER DAVID/IN

```

E2          2      WEINER DAVID A/IN
E3         48 --> WEINER DAVID B/IN
E4          2      WEINER DAVID M/IN
E5          4      WEINER DAVID PAUL/IN
E6          4      WEINER DAVID WILLIAM/IN
E7          1      WEINER DONALD D/IN
E8          7      WEINER DOUGLAS B/IN
E9          5      WEINER DOUGLAS S/IN
E10         1      WEINER EDWARD G/IN
E11         1      WEINER ETHAN S/IN
E12         1      WEINER EUGENE R/IN

=> s e1 or e3
          9 "WEINER DAVID"/IN
         48 "WEINER DAVID B"/IN
L4         57 "WEINER DAVID"/IN OR "WEINER DAVID B"/IN

=> s l4 and (Vpr or viral protein R)
          1263 VPR
          75902 VIRAL
          196519 PROTEIN
         1047992 R
          39 VIRAL PROTEIN R
             (VIRAL(W) PROTEIN(W) R)
L5         33 L4 AND (VPR OR VIRAL PROTEIN R)

=> s l5 and (antibod?)
          118424 ANTIBOD?
L6         33 L5 AND (ANTIBOD?)

=> s l6 and (antibod? (8w) Vpr) or (antibod? (8w) viral protein R)
          118424 ANTIBOD?
          1263 VPR
          39 ANTIBOD? (8W) VPR
          118424 ANTIBOD?
          75902 VIRAL
          196519 PROTEIN
         1047992 R
          39 VIRAL PROTEIN R
             (VIRAL(W) PROTEIN(W) R)
          0 ANTIBOD? (8W) VIRAL PROTEIN R
L7         19 L6 AND (ANTIBOD? (8W) VPR) OR (ANTIBOD? (8W) VIRAL PROTEIN R)

=> s l7 and (antibod?/clm or Vpr/clm or viral protein R/clm)
          36027 ANTIBOD?/CLM
          156 VPR/CLM
          11272 VIRAL/CLM
          57583 PROTEIN/CLM
         298387 R/CLM
          4 VIRAL PROTEIN R/CLM

```

((VIRAL(W) PROTEIN(W) R) /CLM)

L8 18 L7 AND (ANTIBOD?/CLM OR VPR/CLM OR VIRAL PROTEIN R/CLM)

=> d 18,cbib,ab,clm,10-18

L8 ANSWER 10 OF 18 USPATFULL on STN

2003:207377 Cellular receptor for HIV-1 **Vpr** essential for G2/M phase transition of the cell cycle.

Weiner, David B., Merion Station, PA, UNITED STATES

Ayyavoo, Velpandi, Monroeville, PA, UNITED STATES

Mahalingam, Sundarasamy, Birmingham, AL, UNITED STATES

Patel, Mamata, Philadelphia, PA, UNITED STATES

US 2003143735 A1 20030731

APPLICATION: US 2003-208338 A1 20030227 (10)

DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides methods of identifying an anti-H compound by contacting human **Vpr** Interacting Protein (hVIP), or fragment thereof known to interact with **Vpr**, with **Vpr**, or a fragment thereof known to interact with hVIP in the presence of a test compound and comparing the affinity of the hVIP or fragment thereof to the test compound with the affinity of the hVIP or fragment thereof to the **Vpr** or fragment thereof in the absence of the test compound. The present invention provides transgenic non-human mammals comprising a recombinant expression vector that comprises a nucleic acid sequence that encodes hVIP.

CLM What is claimed is:

1. A substantially pure protein having the amino acid sequence of SEQ ID NO:2.
2. A recombinant expression vector comprising a nucleic acid sequence that encodes a protein of claim 1.
3. The recombinant expression vector of claim 2 comprising SEQ ID NO:1.
4. A host cell comprising the recombinant expression vector of claim 3.
5. The host cell of claim 4 comprising a recombinant expression vector that comprises SEQ ID NO:1.
6. An isolated nucleic acid molecule consisting of SEQ ID NO:1, or a fragment thereof having at least 10 nucleotides.
7. The nucleic acid molecule of claim 6 consisting of SEQ ID NO:1.
8. The nucleic acid molecule of claim 6 consisting of a fragment of SEQ ID NO:1 having at least 10 nucleotides.
9. The nucleic acid molecule of claim 6 consisting of a fragment of SEQ ID NO:1 having at least 10 nucleotides.

ID NO:1 having 12-150 nucleotides.

10. The nucleic acid molecule of claim 6 consisting of a fragment ID NO:1 having 15-50 nucleotides.

11. The nucleic acid molecule of claim 6 consisting of a fragment ID NO:1 having 18-30 nucleotides.

12. The nucleic acid molecule of claim 6 consisting of a fragment ID NO:1 having 24 nucleotides.

13. An oligonucleotide molecule comprising a nucleotide sequence complementary to a nucleotide sequence of at least 10 nucleotide ID NO:1.

14. The oligonucleotide molecule of claim 13 consisting of a nucleotide sequence complementary to a nucleotide sequence of 10-150 nucleotides SEQ ID NO:1.

15. The oligonucleotide molecule of claim 13 consisting of a nucleotide sequence complementary to a nucleotide sequence of 18-28 nucleotides SEQ ID NO:1.

16. An isolated **antibody** which binds to an epitope on a protein of claim 1.

17. The **antibody** of claim 16 wherein said **antibody** is a monoclonal **antibody**.

18. A pharmaceutical composition comprising a nucleic acid molecule of claim 6 and a pharmaceutically acceptable carrier.

19. A pharmaceutical composition comprising an oligonucleotide of claim 13 and a pharmaceutically acceptable carrier.

20. A method of making human **Vpr** Interacting Protein comprising: isolating a nucleic acid molecule having SEQ ID NO:1; inserting said nucleic acid molecule into an expression vector; inserting said expression vector into a host cell under conditions in which said protein is expressed; and isolating said human **Vpr** Interacting Protein.

21. A method of inhibiting the expression of human **Vpr** Interacting Protein in a cell comprising contacting said cell with an oligonucleotide complementary to SEQ ID NO:1, or a fragment thereof, whereby said oligonucleotide inhibits expression of said protein.

22. The method of claim 21 wherein said cell is a cancer cell in an animal.

23. The method of claim 21 wherein said oligonucleotide consists

nucleotide sequence complementary to a nucleotide sequence of 10 nucleotides of SEQ ID NO:1.

24. The method of claim 21 wherein said oligonucleotide consists nucleotide sequence complementary to a nucleotide sequence of 18 nucleotides of SEQ ID NO:1.

25. A method of treating an individual who has cancer comprising administering to said individual a therapeutically effective amount of an oligonucleotide complementary to SEQ ID NO:1, or a fragment thereof whereby said oligonucleotide inhibits expression of said protein

26. The method of claim 25 wherein said oligonucleotide consists nucleotide sequence complementary to a nucleotide sequence of 10 nucleotides of SEQ ID NO:1.

27. The method of claim 25 wherein said oligonucleotide consists nucleotide sequence complementary to a nucleotide sequence of 18 nucleotides of SEQ ID NO:1.

28. A method of inhibiting human **Vpr** Interacting Protein activity in a cell comprising contacting said cell with an hVIP-binding fragment thereof

29. The method of claim 28 wherein said cell is in an individual with cancer and said method comprises the step of administering to said individual a therapeutically effective amount of an hVIP-binding fragment of **Vpr**.

L8 ANSWER 11 OF 18 USPTAFULL on STN

2002:230844 Cellular receptor for HIV-1 **Vpr** essential for G2/M phase transition of the cell cycle.

Weiner, David B., Merion Station, PA, United States

Ayyavoo, Velpandi, Monroeville, PA, United States

Mahalingam, Sundarasamy, Birmingham, AL, United States

Patel, Mamata, Philadelphia, PA, United States

The Trustees of the University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)

US 6448078 B1 20020910

WO 9919359 19990422

APPLICATION: US 2000-529245 20001017 (9)

WO 1998-US21432 19981009 20001017 PCT 371 date

DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to substantially pure Human **V** Interacting Protein (hVIP), and fragments thereof. Also disclosed are isolated nucleic acid molecules that encode hVIP, or a fragment thereof; nucleic acid probes and primers directed to nucleic acid molecules that encode hVIP, or a fragment thereof; oligonucleotide molecules that consist of a nucleotide sequence complementary to a portion of the

nucleotide sequence that encodes hVIP; vectors comprising nuclei molecules encoding hVIP; recombinant expression vectors that com nucleic acid sequences that encode hVIP; host cells that compris recombinant expression vectors which include nucleic acid sequen encode hVIP; genetic therapy vectors comprising nucleic acid mol encoding hVIP; isolated **antibody** which binds to an epitope on hV pharmaceutical compositions comprising a pharmaceutically accept carrier and nucleic acid molecules complementary to a portion of methods of making hVIP; and methods of inhibiting expression of oligonucleotides complementary to a portion of the nucleotide se that encodes hVIP.

CLM

What is claimed is:

1. An isolated **antibody** which binds to an epitope on a protein h the amino acid sequence of SEQ ID NO:2.
2. The **antibody** of claim 1 wherein said **antibody** is a monoclonal **antibody**.
3. A method of inhibiting the expression of human **Vpr** Interacting Protein in a cell comprising contacting said cell with an oligonucleotide complementary to SEQ ID NO:1, or a fragment thereof whereby said oligonucleotide inhibits expression of said protein
4. The method of claim 3 wherein said cell is a cancer cell in a animal.
5. The method of claim 3 wherein said oligonucleotide consists of nucleotide sequence complementary to a nucleotide sequence of 10 nucleotides of SEQ ID NO:1.
6. The method of claim 3 wherein said oligonucleotide consists of nucleotide sequence complementary to a nucleotide sequence of 18 nucleotides of SEQ ID NO:1.
7. A method of treating an individual who has cancer comprising administering to said individual a therapeutically effective amount of an oligonucleotide complementary to SEQ ID NO:1, or a fragment thereof whereby said oligonucleotide inhibits expression of said protein
8. The method of claim 7 wherein said oligonucleotide consists of nucleotide sequence complementary to a nucleotide sequence of 10 nucleotides of SEQ ID NO:1.
9. The method of claim 7 wherein said oligonucleotide consists of nucleotide sequence complementary to a nucleotide sequence of 18 nucleotides of SEQ ID NO:1.
10. A method of inhibiting human **Vpr** Interacting Protein activity in a cell comprising contacting said cell with an hVIP-binding fragment thereof

11. The method of claim 10 wherein said cell is in an individual cancer and said method comprises the step of administering to said individual a therapeutically effective amount of an hVIP-binding fragment of **Vpr**.

L8 ANSWER 12 OF 18 USPTAFULL on STN

2001:4875 Cellular receptor for HIV-1 **Vpr** essential for G2/M phase.

Weiner, David B., Merion, PA, United States

Ayyavoo, Velpandi, Havertown, PA, United States

Mahalingam, Sundarasamy, Birmingham, AL, United States

Patel, Mamata, Philadelphia, PA, United States

The Trustees of the University of Pennsylvania, Philadelphia, PA, U States (U.S. corporation)

US 6172201 B1 20010109

APPLICATION: US 1999-418175 19991013 (9)

PRIORITY: US 1997-55754P 19970814 (60)

DOCUMENT TYPE: Patent; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to substantially pure human **V** Interacting Protein (hVIP), and fragments thereof. Also disclose isolated nucleic acid molecules that encode hVIP, or a fragment nucleic acid probes and primers directed to nucleic acid molecules that encode hVIP, or a fragment thereof; oligonucleotide molecules that consist of a nucleotide sequence complementary to a portion of the nucleotide sequence that encodes hVIP; vectors comprising nucleic acid molecules encoding hVIP; recombinant expression vectors that comprise nucleic acid sequences that encode hVIP; host cells that comprise recombinant expression vectors which include nucleic acid sequences that encode hVIP; genetic therapy vectors comprising nucleic acid molecules encoding hVIP; isolated **antibody** which binds to an epitope on hVIP; pharmaceutical compositions comprising a pharmaceutically acceptable carrier and nucleic acid molecules complementary to a portion of the nucleotide sequence that encodes hVIP; and methods of inhibiting expression of oligonucleotides complementary to a portion of the nucleotide sequence that encodes hVIP.

CLM What is claimed is:

1. An isolated **antibody** which binds to an epitope on a protein having the amino acid sequence of SEQ ID NO:2.

2. The **antibody** of claim 1 wherein said **antibody** is a monoclonal **antibody**.

3. The **antibody** of claim 1 wherein the **antibody** is an **antibody**

4. The **antibody** of claim 3 wherein the **antibody** fragment is a F fragment.

5. The **antibody** of claim 3 wherein the **antibody** fragment is a F(ab)₂ fragment.

6. A hybridoma cell line which produces **antibodies** according to

L8 ANSWER 13 OF 18 USPATFULL on STN

2000:57881 Cellular receptor for HIV-1 **VPR** essential for G2/M phase transition of the cell cycle.

Weiner, David B., Merion, PA, United States

Ayyavoo, Velpandi, Havertown, PA, United States

Mahalingam, Sundarasamy, Birmingham, AL, United States

Patel, Mamata, Philadelphia, PA, United States

The Trustees of the University of Pennsylvania, Philadelphia, PA, U States (U.S. corporation)

US 6060587 20000509

APPLICATION: US 1997-949202 19971010 (8)

PRIORITY: US 1997-55754P 19970814 (60)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to substantially pure human **V** Interacting Protein (hVIP), and fragments thereof. Also disclose isolated nucleic acid molecules that encode hVIP, or a fragment nucleic acid probes and primers directed to nucleic acid molecules that encode hVIP, or a fragment thereof; oligonucleotide molecules that consist of a nucleotide sequence complementary to a portion of the nucleotide sequence that encodes hVIP; vectors comprising nucleic acid molecules encoding hVIP; recombinant expression vectors that comprise nucleic acid sequences that encode hVIP; host cells that comprise recombinant expression vectors which include nucleic acid sequences that encode hVIP; genetic therapy vectors comprising nucleic acid molecules encoding hVIP; isolated **antibody** which binds to an epitope on hVIP; pharmaceutical compositions comprising a pharmaceutically acceptable carrier and nucleic acid molecules complementary to a portion of the nucleotide sequence that encodes hVIP; and methods of inhibiting expression of oligonucleotides complementary to a portion of the nucleotide sequence that encodes hVIP.

CLM What is claimed is:

1. A substantially pure protein having the amino acid sequence of SEQ ID NO:2.
2. A recombinant expression vector comprising a nucleic acid sequence that encodes the protein of claim 1.
3. A host cell comprising the recombinant expression vector of claim 2.
4. The host cell of claim 3 comprising a recombinant expression vector that comprises SEQ ID NO:1.
5. An isolated nucleic acid molecule consisting of SEQ ID NO:1, or a fragment thereof having at least 10 nucleotides.

6. The nucleic acid molecule of claim 5 consisting of a fragment ID NO:1 having at least 10 nucleotides.
7. The nucleic acid molecule of claim 5 consisting of a fragment ID NO:1 having 12-150 nucleotides.
8. The nucleic acid molecule of claim 5 consisting of a fragment ID NO:1 having 15-50 nucleotides.
9. The nucleic acid molecule of claim 5 consisting of a fragment ID NO:1 having 18-30 nucleotides.
10. The nucleic acid molecule of claim 5 consisting of a fragment ID NO:1 having 24 nucleotides.
11. An oligonucleotide molecule comprising a nucleotide sequence complementary to a nucleotide sequence of at least 10 nucleotide ID NO:1.
12. The oligonucleotide molecule of claim 11 consisting of a nucleotide sequence complementary to a nucleotide sequence of 10-150 nucleotides SEQ ID NO:1.
13. The oligonucleotide molecule of claim 11 consisting of a nucleotide sequence complementary to a nucleotide sequence of 18-28 nucleotides SEQ ID NO:1.
14. A pharmaceutical composition comprising: a) a nucleic acid molecule that comprises SEQ ID NO: 1 or a fragment from the coding region having at least 100 nucleotides; and b) a pharmaceutically acceptable carrier.
15. A pharmaceutical composition comprising: a) an oligonucleotide that comprises a nucleotide sequence complementary to a nucleotide sequence of at least 10 nucleotides of the coding region of SEQ ID NO: 1; and b) a pharmaceutically acceptable carrier.
16. A method of making human Vpr Interacting Protein comprising: isolating a nucleic acid molecule having SEQ ID NO:1; inserting said nucleic acid molecule into an expression vector; inserting said expression vector into a host cell under conditions in which said protein is expressed; and isolating said human Vpr Interacting Protein.
17. A plasmid comprising a nucleic acid sequence that encodes a protein that has the amino acid sequence of SEQ ID NO:2.
18. The plasmid of claim 17 comprising SEQ ID NO:1.
19. An isolated nucleic acid molecule consisting of SEQ ID NO:1.

20. A recombinant expression vector comprising the nucleic acid of claim 19.
21. A host cell comprising the recombinant expression vector of 20.
22. An isolated nucleic acid molecule consisting of a fragment of coding region of SEQ ID NO: 1 having at least 10 contiguous nucleotides of SEQ ID NO: 1.
23. An isolated nucleic acid molecule consisting of a fragment of coding region of SEQ ID NO: 1 having 12-150 contiguous nucleotides of SEQ ID NO: 1.
24. An isolated nucleic acid molecule consisting of a fragment of coding region of SEQ ID NO: 1 having 15-50 contiguous nucleotides of SEQ ID NO: 1.
25. An isolated nucleic acid molecule consisting of a fragment of coding region of SEQ ID NO: 1 having 18-30 contiguous nucleotides of SEQ ID NO: 1.
26. An isolated nucleic acid molecule consisting of a fragment of coding region of SEQ ID NO: 1 having 24 contiguous nucleotides of SEQ ID NO: 1.
27. An isolated nucleic acid molecule comprising a fragment of SEQ ID NO: 1 having 100 contiguous nucleotides of SEQ ID NO: 1.
28. The isolated nucleic acid molecule of claim 27 comprising a fragment of the coding region of SEQ ID NO: 1 having 100 contiguous nucleotides of SEQ ID NO: 1.
29. An isolated nucleic acid molecule comprising a fragment of SEQ ID NO: 1 having 150 contiguous nucleotides of SEQ ID NO: 1.
30. The isolated nucleic acid molecule of claim 29 comprising a fragment of the coding region of SEQ ID NO: 1 having 150 contiguous nucleotides of SEQ ID NO: 1.
31. The pharmaceutical composition of claim 14 wherein said nucleic acid molecule comprises a fragment of SEQ ID NO:1 having at least 150 contiguous nucleotides of SEQ ID NO:1.
32. A pharmaceutical composition comprising: a) a nucleic acid molecule that consists of SEQ ID NO: 1 or a fragment of SEQ ID NO:1 having at least 10 contiguous nucleotides of SEQ ID NO:1; and b) a pharmaceutically acceptable carrier.
33. The pharmaceutical composition of claim 32 wherein said fragment

SEQ ID NO:1 has 12-150 contiguous nucleotides of SEQ ID NO:1.

34. The pharmaceutical composition of claim 14 wherein said frag
SEQ ID NO:1 has 15-50 contiguous nucleotides of SEQ ID NO:1.

35. The pharmaceutical composition of claim 14 wherein said frag
SEQ ID NO:1 has 18-30 contiguous nucleotides of SEQ ID NO:1.

L8 ANSWER 14 OF 18 USPATFULL on STN

1999:24450 Identification of compounds that modulate HIV-1 **vpr** protein

Weiner, David B., Merion, PA, United States

Levy, David Nathan, Philadelphia, PA, United States

Trustees of The University of Pennsylvania, Philadelphia, PA, United States
(U.S. corporation)The Wistar Institute, Philadelphia, PA, United States
(U.S. corporation)

US 5874225 19990223

APPLICATION: US 1993-19601 19930219 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed toward methods of identifying
compounds which inhibit the human immunodeficiency virus (HIV)
protein R (Vpr) from stimulating the differentiation of
undifferentiated cells. This invention takes advantage of the
observation that cell lines from rhabdomyosarcomas, which are of
muscle origin, have been used as models of CD4-independent HIV
infection. These cell lines can be induced to differentiate in vitro.
The **vpr** gene of HIV-1 is sufficient for the differentiation of the
human rhabdomyosarcoma cell line TE671. Differentiated cells are
characterized by great enlargement, altered morphology, lack of
replication, and high level expression of the muscle-specific p
myosin. Morphological differentiation and inhibition of proliferation
of other transformed cell lines following **vpr** expression was also
observed. This invention also relates toward methods of identifying
compounds which inhibit HIV **Vpr** binding to Gag. These screening
methods should facilitate the identification and development of
antiviral agents.

CLM What is claimed is:

1. An in vitro method of identifying compounds that are capable
of inhibiting HIV-1 **Vpr**-mediated differentiation of undifferentiated
cells comprising the following steps: (i) contacting undifferentiated
cells with HIV-1 **Vpr** in the presence or absence of a test compound
and, (ii) determining whether said cells cease proliferating and
cellular differentiation markers in the presence or absence of a
compound; wherein the presence of cellular proliferation and absence
of differentiation markers in the test sample is indicative of said
compound being capable of inhibiting HIV-1 **Vpr**-mediated
differentiation of undifferentiated cells.

2. The method of claim 1 wherein said undifferentiated cells are selected from the group consisting of: solid muscle tumor alveolar rhabdomyosarcoma cell line RD, solid muscle tumor alveolar rhabdomyosarcoma cell line TE671, osteosarcoma cell line D17, osteosarcoma cell line MG63, osteosarcoma cell line HOS-TE86, myeloid lineage cell line KG-1, myeloid lineage cell line THP-1, myeloid cell line PLB973, human glioblastoma cell line U-138MG, human glioblastoma/astrocytoma cell line U373MG, and human glioblastoma/astrocytoma cell line U87-MG.

3. An in vitro method of identifying compounds that are capable of inhibiting HIV-1 **Vpr**-mediated suppression of cellular proliferation comprising the following steps: (I) contacting proliferating cells with HIV-1 **Vpr** in the presence or absence of a test compound; and, (ii) determining whether said cells cease proliferating in the presence or absence of said test compound; wherein the presence of cellular proliferation in the test sample is indicative of said compound being capable of inhibiting HIV-1 **Vpr**-mediated suppression of cellular proliferation.

4. The method of claim 3 wherein said proliferating cells are selected from the group consisting of: solid muscle tumor alveolar rhabdomyosarcoma cell line RD, solid muscle tumor alveolar rhabdomyosarcoma cell line TE671, osteosarcoma cell line D17, osteosarcoma cell line MG63, osteosarcoma cell line HOS-TE86, myeloid lineage cell line KG-1, myeloid lineage cell line THP-1, myeloid cell line PLB973, human glioblastoma cell line U-138MG, human glioblastoma/astrocytoma cell line U373MG, and human glioblastoma/astrocytoma cell line U87-MG.

5. An in vitro method for the identification of compounds capable of inhibiting HIV-1 **Vpr** binding to HIV-1 Gag comprising the following steps: (I) contacting, in the presence or absence of a test compound, HIV-1 **Vpr** and Gag; and (ii) determining the level of binding between HIV-1 **Vpr** and Gag, wherein a reduction in binding in the presence of the test compound is indicative of said compound being capable of inhibiting HIV-1 **Vpr** binding to Gag.

6. The method of claim 5 wherein said binding level is determined by the addition of a labeled **antibody**.

7. The method of claim 5 wherein said HIV-1 **Vpr** and Gag are produced in eukaryotic cells.

8. The method of claim 5 wherein said HIV-1 **Vpr** and Gag are produced in insect cells.

9. The method of claim 5 comprising the following steps: (I) contacting, in the presence or absence of a test compound, eukaryotically expressed HIV-1 **Vpr** and Gag, wherein said **Vpr** is attached to a solid support.

(ii) washing the mixture of step (I) to remove unbound Gag prote
(iii) determining the level of binding between HIV-1 **Vpr** and Ga
through the addition of a Gag-specific labeled **antibody**, wherei
reduction in binding in the presence of the test compound is ind
of said compound being capable of inhibiting HIV-1 **Vpr** binding

10. The method of claim 9 wherein said HIV-1 **Vpr** and Gag are pr
in insect cells.

11. The method of claim 5 comprising the following steps: (I)
contacting, in the presence or absence of a test compound,
eukaryotically expressed HIV-1 **Vpr** and Gag, wherein said Gag is
attached to a solid support; (ii) washing the mixture of step (I
remove unbound **Vpr** protein; and, (iii) determining the level of
binding between HIV-1 **Vpr** and Gag through the addition of a
Vpr-specific labeled **antibody**, wherein a reduction in binding in
presence of the test compound is indicative of said compound bei
capable of inhibiting HIV-1 **Vpr** binding to Gag.

12. The method of claim 11 wherein said HIV-1 **Vpr** and Gag are p
in insect cells.

L8 ANSWER 15 OF 18 USPATFULL on STN

1998:82540 **VPR** receptor protein.

Weiner, David B., Merion, PA, United States

Levy, David Nathan, Boston, MA, United States

Refaeli, Yosef, Boston, MA, United States

The Trustees of the University of Pennsylvania, Philadelphia, PA, U
States (U.S. corporation)

US 5780238 19980714

WO 9516705 19950622

APPLICATION: US 1996-652572 19961024 (8)

WO 1994-US14532 19941215 19961024 PCT 371 date 19961024 PCT 102(e
DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A human receptor protein which binds to the human immunodeficien
(HIV) **viral protein R (vpr)** is disclosed. Pharmaceutical
compositions that comprise the receptor protein, compositions us
produce the receptor protein and methods of making and using the
receptor protein are disclosed.

CLM What is claimed is:

1. Essentially pure **viral protein R** receptor protein characteriz
by a molecular weight of about 41 kD as determined using 12% SDS
an ability to bind to **viral protein R** and solubility in Triton,
a fragment of said **viral protein R** receptor protein which binds
viral protein R.

2. The protein of claim 1 wherein said protein is characterized
molecular weight of about 41 kD as determined using 12% SDS-PAG

ability to bind to **viral protein R** and solubility in Triton.

3. The protein of claim 1 wherein said protein is a fragment of protein which has a molecular weight of about 41 kD as determined by 12% SDS-PAGE, said fragment having the ability to bind to **viral protein R** and solubility in Triton.

4. A method of identifying compounds which inhibit binding of **viral protein R** to the viral protein receptor protein of claim 1 which comprises the steps of: a) contacting in the presence of a test compound, **viral protein R** protein or a fragment thereof and said **viral protein R** receptor protein or a fragment thereof, wherein the absence of said test compound said **viral protein R** protein or said fragment thereof binds to said **viral protein R** receptor protein or said fragment thereof; b) determining the level of binding and c) comparing that level to the level of binding that occurs when said **viral protein R** protein and said **viral protein R** receptor protein are contacted in the absence of a test compound, wherein a decrease in binding levels in the presence of said test compound indicates that the test compound is a compound which inhibits binding of **viral protein R** protein to the **viral protein R** receptor protein of claim 1.

5. A kit for identifying compounds which inhibit binding of **viral protein R** protein to the **viral protein R** receptor protein of claim 1 which comprises a) a first container which contains **viral protein R** protein or a fragment thereof which binds to **viral protein R** receptor protein or a fragment thereof, and b) a second container which contains said **viral protein R** receptor protein or a fragment thereof which binds to **viral protein R** protein or a fragment thereof.

L8 ANSWER 16 OF 18 USPTAFULL on STN

1998:82523 Methods and compositions for inhibiting HIV replication.

Weiner, David B., Merion, PA, United States

Refaeli, Yosef, Boston, MA, United States

Levy, David N., Birmingham, AL, United States

Trustees of the University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)

US 5780220 19980714

APPLICATION: US 1995-382873 19950203 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for treating an individual exposed to or infected with HIV, disclosed which comprises administering to said individual a therapeutically effective amount of one or more compounds which inhibit or prevent replication of said HIV by interfering with the replication or other essential functions of **Vpr** expressed by said HIV, by interactively blocking the **Vpr** target in human cells, and thereby

preventing translocation of the **Vpr**/target complex from the cytosol of said human cells to the nuclei of said cells, where **Vpr** carries activities essential to replication of HIV. In preferred embodiment the compound or compounds which interactively block the target are steroid hormone receptor antagonists, glucocorticoid receptor antagonists, or glucocorticoid receptor Type II antagonists, especially mifepristone (RU-486). Pharmaceutical compositions comprising the compounds, as well as a method for identifying them and a kit for use therein, are also disclosed.

CLM What is claimed is:

1. A method for treating a human individual exposed to or infected with HIV comprising the steps of identifying said individual, and administering to said individual a therapeutically effective amount of mifepristone to inhibit or prevent replication of said HIV by inhibiting cytosolic-nuclear translocation of a complex comprising HIV **Vpr** protein and Rip-1 protein in an HIV infected cell of said individual.

2. A method according to claim 1 further comprising coadministering to said individual one or more therapeutic agents useful for treating HIV infected individuals, selected from the group consisting of zidovudine (AZT), acyclovir, ganciclovir, foscarnet, interferon alpha-2a, and interferon alpha-2b.

3. A pharmaceutical composition for treatment of a human individual exposed to or infected with HIV comprising a therapeutically effective amount of mifepristone, one or more therapeutic agents useful for treating HIV infected individuals, selected from the group consisting of zidovudine (AZT), acyclovir, ganciclovir, foscarnet, interferon alpha-2a, and interferon alpha-2b; and a pharmaceutically acceptable carrier therefor.

L8 ANSWER 17 OF 18 USPTAFULL on STN

1998:64981 Methods for the identification of compounds capable of inducing nuclear translocation of a receptor complex comprising the glucocorticoid receptor type II and **viral protein R** interacting protein.

Weiner, David B., Merion, PA, United States

Refaeli, Yosef, Boston, MA, United States

The Trustees of the University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)

US 5763190 19980609

APPLICATION: US 1994-309644 19940921 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Human immunodeficiency virus (HIV)-1, HIV-2, and simian immunodeficiency virus contain, in addition to the canonical gag/pol/env genes, additional small open reading frames encoding gene products, including the 96-amino acid 15-kDa virion associated HIV-1 **Vpr** gene product. Conservation of the **vpr** open reading frame in primate lentivirus suggests that **vpr** is critical to viral replication. A biological

active recombinant HIV-1 **Vpr** protein was employed as a ligand to identify its cellular targets. A novel 41-kDa cytosolic protein identified and termed the **viral protein R** interacting protein, Rip-1. Rip-1 displays a wide tissue distribution, including relevant targets of HIV infection. **Vpr** protein induced nuclear translocation of Rip-1, as did glucocorticoid receptor (GR)-II-stimulating steroid. **Vpr** and Rip-1 coimmunoprecipitated with the human GR as part of the receptor complex. The present invention discloses methods for the identification of compounds capable of inducing GR-II/Rip-1 receptor complex cytosolic to nuclear translocation.

CLM What is claimed is:

1. An in vitro method of identifying compounds that induce glucocorticoid receptor type II (GR-II) and **viral protein R** interacting protein (Rip-1) complex translocation comprising the following steps: a) preparing cells expressing Rip-1 and the GR wherein Rip-1 and GR-II are capable of forming a cytosolic Rip-receptor complex; b) contacting said cells with a test compound of inducing Rip-1/GR-II receptor complex cytoplasmic to nuclear translocation; c) detecting the level of Rip-1/GR-II receptor complex cytoplasmic to nuclear translocation in said cells in the presence of the test compound; and, d) performing a control assay that detects the level of Rip-1/GR-II receptor complex nuclear translocation in the absence of said test compound; wherein detection of a higher level of cytoplasmic to nuclear translocation of the Rip-1/GR-II receptor complex is indicative of said compound being capable of inducing Rip-1/receptor complex translocation.
2. The method of claim 1 wherein Rip-1/GR-II receptor complex nuclear translocation is detected through the subcellular fractionation of cells into soluble and insoluble antigen-containing fractions, by the addition of Rip-1-specific **antibodies** to each fraction.
3. The method of claim 2 wherein said **antibodies** contain a radiolabel, fluorescent label, or enzymatic label.
4. The method of claim 2 wherein the soluble and insoluble antigen-containing fractions are attached to a solid support.
5. An in vitro method of inducing glucocorticoid receptor type II (GR-II) and **viral protein R** interacting protein (Rip-1) complex nuclear translocation in cells comprising the following steps: a) preparing cells expressing Rip-1 and GR-II wherein said protein is capable of forming a cytosolic Rip-1/GR-II receptor complex; and b) contacting said cells with the human immunodeficiency virus type 1 (HIV-1) **Vpr** protein under conditions wherein said **Vpr** protein binds to the cytosolic Rip-1/GR-II receptor complex thereby generating a **Vpr**/Rip-1/GR-II complex that subsequently undergoes cytoplasmic to nuclear translocation.

L8 ANSWER 18 OF 18 USPATFULL on STN

97:51852 Method and kit for identification of antiviral agents capable abrogating HIV **Vpr**-Rip-1 binding interactions.

Weiner, David B., Merion, PA, United States

Refaeli, Yosef, Boston, MA, United States

Levy, David N., Birmingham, AL, United States

The Trustees of the University of Pennsylvania, Philadelphia, PA, U States (U.S. corporation)

US 5639598 19970617

APPLICATION: US 1994-246177 19940519 (8)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Human and simian immunodeficiency viruses (HIV/SIVs) contain, in addition to the canonical gag/pol/env genes, additional small op reading frames (ORFs) encoding gene products, including the 96-acid 15-kDa virion-associated HIV-1 **Vpr** gene product. **Vpr** funct as a regulator of cellular processes related to HIV replication. biologically active recombinant HIV-1 **Vpr** protein was employed ligand to identify its cognate cellular target(s). A novel 41-k cytosolic **viral protein R** interacting protein, designated Rip-1 was identified using the recited assay. Rip-1 displays a wide-t distribution, including relevant targets of HIV infection. HIV-induced nuclear translocation of Rip-1. This invention provides biochemical reagents and methods that will facilitate the identi of antiviral agents.

CLM What is claimed is:

1. An in vitro method of identifying a compound which is capable preventing HIV-1 **Vpr** from forming a complex with Rip-1 comprisi following steps: a) contacting **Vpr** and Rip-1 in the presence of compound; b) determining the level of **Vpr**/Rip-1 complex formati comparing the level of **Vpr**/Rip-1 complex formation in step (b) t level of **Vpr**/Rip-1 binding that occurs in the absence of said te compound.

2. The method of claim 1 wherein said level of **Vpr**/Rip-1 comple formation is determined by immunoassay.

3. An in vitro method of identifying a compound which is capable preventing HIV-1 **Vpr** from forming a complex with Rip-1 comprisi following steps: a) immobilizing Rip-1 to a solid support; b) co said immobilized Rip-1 with **Vpr** and a test compound; c) measurin **Vpr** binding to immobilized Rip-1 through the administration of **Vpr**-specific **antibodies**; and, d) comparing the level of **Vpr**/Rip binding in step (c) to the level of **Vpr**/Rip-1 binding that occu the absence of said test compound.

4. An in vitro method of identifying a compound which is capable preventing HIV-1 **Vpr** from forming a complex with Rip-1 comprisi following steps: a) immobilizing **Vpr** to a solid support; b) cont said immobilized **Vpr** with Rip-1 and a test compound; c) measurin

Rip-1 binding to immobilized **Vpr** through the administration of Rip-1-specific **antibodies**; and, d) comparing the level of **Vpr**/Rip-1 binding in step (c) to the level of **Vpr**/Rip-1 binding that occurs in the absence of said test compound.

5. An in vitro method for the identification of compounds capable of inhibiting HIV-1 **Vpr** from forming a complex with Rip-1, said method comprising the following steps: a) contacting a culture of HIV-1-infected cells with a test compound; b) determining the level of **Vpr**/Rip-1 binding in said HIV-1-infected cells; and, c) comparing the level of **Vpr**/Rip-1 binding in step (b) to the level of **Vpr**/Rip-1 binding that occurs in HIV-1-infected cells cultured in the absence of said test compound.

6. An in vitro method for the identification of compounds capable of inhibiting HIV-1 viral replication through the abrogation of HIV-1 **Vpr**/Rip-1 complex cytoplasmic to nuclear translocation, said method comprising the following steps: a) contacting a culture of HIV-1-infected cells with a test compound; b) determining the level of cytoplasmic to nuclear translocation of HIV-1 **Vpr**/Rip-1 complex; and, c) comparing the level of cytoplasmic to nuclear translocation of HIV-1 **Vpr**/Rip-1 complexes in the presence of said test compound to the level of cytoplasmic to nuclear translocation of HIV-1 **Vpr**/Rip-1 complexes that occurs in HIV-1-infected cells cultured in the absence of said test compound.

7. A method according to claim 6 further comprising the following steps: d) determining the level of p24 antigen produced in HIV-1 infected cells cultured in the presence of said test compound; e) comparing the level of p24 antigen produced in HIV-1-infected cells cultured in the presence of said test compound to the level of p24 antigen produced by HIV-1-infected cells cultured in the absence of said test compound wherein said comparison results in the identification of compounds capable of inhibiting HIV-1 viral replication.

8. An in vitro method for the identification of glucocorticoid receptor antagonists capable of inhibiting HIV-1 **Vpr** from forming a complex with Rip-1, said method comprising the following steps: a) contacting a culture of HIV-1-infected cells with a glucocorticoid receptor antagonist; b) determining the level of **Vpr**/Rip-1 binding in said HIV-1 infected cells; and, c) comparing the level of **Vpr**/Rip-1 binding in step (b) to the level of **Vpr**/Rip-1 binding that occurs in HIV-1-infected cells cultured in the absence of said test compound.

9. An in vitro method for the identification of glucocorticoid receptor antagonists capable of inhibiting HIV-1 viral replication through abrogation of HIV-1 **Vpr**/Rip-1 complex cytoplasmic to nuclear translocation, said method comprising the following steps: a) contacting a culture of HIV-1-infected cells with a glucocorticoid receptor antagonist; b) determining the level of cytoplasmic to nuclear

translocation of HIV-1 Vpr/Rip-1 complexes; and, c) comparing the level of cytoplasmic to nuclear translocation of HIV-1 Vpr/Rip-1 complexes in the presence of said test compound to the level of cytoplasmic to nuclear translocation of HIV-1 Vpr/Rip1 complexes occurs in HIV-1-infected cells cultured in the absence of said test compound.

=> d 18,cbib,ab,clm,1-9

L8 ANSWER 1 OF 18 USPTAFULL on STN

2005:63067 Targeted particles and methods of using the same.

Weiner, David B., Merion Station, PA, UNITED STATES

Muthumani, Karuppiiah, Cherry Hill, NJ, UNITED STATES

Zhang, Donghui, Philadelphia, PA, UNITED STATES

Ramathan, Mathura P., Ardmore, PA, UNITED STATES

US 2005054104 A1 20050310

APPLICATION: US 2004-478896 A1 20040830 (10)

WO 2002-US16681 20020528

PRIORITY: US 2001-293683P 20010525 (60)

DOCUMENT TYPE: Utility; APPLICATION.

AB Drug delivery compositions and methods of delivering compounds disclosed. Vaccines and methods of immunizing individuals are disclosed. Compositions for drug delivery including gene therapy and methods of treating individuals using such compositions are disclosed.

CLM What is claimed is:

1. A method of introducing a compound into a cell that expresses molecules, said method comprising contacting the cell with a non-cellular particle that comprises the compound and a Flt-3 ligand.

2. The method of claim 1 wherein the compound is a nucleic acid or protein.

3. The method of claim 1 wherein the compound is DNA.

4. The method of claim 1 wherein the compound is DNA that comprises nucleotide sequences that encodes a protein operably linked to regulatory elements functional in the cell.

5. The method of claim 1 wherein the compound is DNA that comprises nucleotide sequences that encodes an immunogenic protein operably linked to regulatory elements functional in the cell.

6. The method of claim 1 wherein the compound is DNA that comprises nucleotide sequences that encodes a non-immunogenic protein operably linked to regulatory elements functional in the cell.

7. The method of claim 1 wherein the compound is DNA that comprises nucleotide sequences that encodes a protein operably linked to

regulatory elements derived from AAV, adenovirus or alphavirus.

8. The method of claim 1 wherein the compound is DNA that comprises nucleotide sequences that encodes a protein operably linked to regulatory elements derived from AAV, adenovirus or alphavirus, further comprising a packaging signal to facilitate its incorporation into said particle.

9. The method of claim 1 wherein the compound is a viral protein

10. The method of claim 1 wherein the compound is a fusion protein comprising an HIV **Vpr** portion which facilitates incorporation of fusion protein into said particle.

11. The method of claim 10 wherein fusion protein comprising a protease cleavage site between said **Vpr** portion and a biologically active portion.

12. The method of claim 11 wherein the protease cleavage site is a cleavage site recognized by HIV-1 protease.

13. The method of claim 10 wherein fusion protein comprising a biologically active portion selected from the group consisting of transcription factors, growth factors, cytokines, chemokines, transport proteins and processing proteins.

14. The method of claim 13 wherein fusion protein comprising a biologically active portion selected from the group consisting of transcription factor Tbet, transcription factor Tgata, cytokine chemokine Rantes, transport protein p70 and processing protein T

15. The method of claim 1 wherein the particle is a viral particle, protein complex, a liposome or a cationic amphiphile/DNA complex

16. The method of claim 1 wherein the particle comprises a fusion protein comprising Flt-3 ligand or a FLT-3 binding fragment, the transmembrane and cytoplasmic regions of HIV-1 gp41.

17. A non-cellular particle that comprises a fusion protein comprising Flt-3 ligand or a FLT-3 binding fragment thereof.

18. The particle of claim 17 further comprising a nucleic acid and/or fusion protein.

19. The particle of claim 18 comprising DNA.

20. The particle of claim 19 wherein the DNA comprises a nucleotide sequence that encodes a protein operably linked to regulatory elements functional in the cell.

21. The particle of claim 19 wherein the DNA comprises a nucleot sequences that encodes an immunogenic protein operably linked to regulatory elements functional in the cell.
22. The particle of claim 19 wherein the DNA comprises a nucleot sequences that encodes an non-immunogenic protein operably linke regulatory elements functional in the cell.
23. The particle of claim 19 wherein the DNA comprises a nucleot sequences that encodes a protein operably linked to regulatory e derived from AAV, adenovirus or alphavirus.
24. The particle of claim 19 wherein the DNA comprises a nucleot sequences that encodes a protein operably linked to regulatory e derived from AAV, adenovirus or alphavirus, said DNA further com a packaging signal to facilitate its incorporation into said par
25. The particle of claim 18 comprising a fusion protein.
26. The particle of claim 18 wherein the fusion protein comprise **Vpr** portion which facilitate incorporation of said fusion protei said particle.
27. The particle of claim 18 wherein the fusion protein comprise protease cleavage site between said **Vpr** portion and a biological active portion.
28. The particle of claim 27 wherein the protease cleavage site cleavage site recognized by HIV-1 protease.
29. The particle of claim 18 wherein fusion protein comprising a biologically active portion selected from the group consisting o transcription factors, growth factors, cytokines, chemokines, tr proteins and processing proteins.
30. The particle of claim 29 wherein fusion protein comprising a biologically active portion selected from the group consisting o transcription factor Tbet, transcription factor Tgata, cytokine chemokine Rantes, transport protein p70 and processing protein T
31. The particle of claim 17 wherein the particle is a viral par protein complex, a liposome or a cationic amphiphile/DNA complex
32. The particle of claim 17 wherein the particle comprises a fu protein comprising Flt-3 ligand or a FLT-3 binding fragment the the transmembrane and cytoplasmic regions of HIV-1 gp41.
33. The method of immunizing an individual comprising administer particle of claim 30.

34. The method of treating an individual for autoimmune disease comprising administering a particle of claim 30.
35. A non-cellular particle that comprises a fusion protein comprising a **Vpr** portion and a biologically active non-**Vpr** portion.
36. The particle of claim 35 wherein the fusion protein comprises a **Vpr** portion which facilitates incorporation of said fusion protein into said particle.
37. The particle of claim 35 wherein the fusion protein comprises a protease cleavage site between said **Vpr** portion and a biologically active portion.
38. The particle of claim 37 wherein the protease cleavage site is a cleavage site recognized by HIV-1 protease.
40. The particle of claim 35 wherein the fusion protein comprises a biologically active portion selected from the group consisting of transcription factors, growth factors, cytokines, chemokines, transport proteins and processing proteins.
41. The particle of claim 40 wherein the fusion protein comprises a biologically active portion selected from the group consisting of transcription factor Tbet, transcription factor Tgata, cytokine chemokine Rantes, transport protein p70 and processing protein T.
42. The particle of claim 35 further comprising a nucleic acid molecule and/or a fusion protein.
43. The particle of claim 42 comprising DNA.
44. The particle of claim 43 wherein the DNA comprises a nucleotide sequence that encodes a protein operably linked to regulatory elements functional in the cell.
45. The particle of claim 43 wherein the DNA comprises a nucleotide sequence that encodes an immunogenic protein operably linked to regulatory elements functional in the cell.
46. The particle of claim 43 wherein the DNA comprises a nucleotide sequence that encodes a non-immunogenic protein operably linked to regulatory elements functional in the cell.
47. The particle of claim 43 wherein the DNA comprises a nucleotide sequence that encodes a protein operably linked to regulatory elements derived from AAV, adenovirus or alphavirus.
48. The particle of claim 43 wherein the DNA comprises a nucleotide sequence that encodes a protein operably linked to regulatory elements

derived from AAV, adenovirus or alphavirus, said DNA further comprising a packaging signal to facilitate its incorporation into said particle.

49. The particle of claim 35 comprising a costimulatory ligand or fusion protein comprising costimulatory ligand portion.

50. The particle of claim 35 wherein the particle is an HIV viral particle.

51. The particle of claim 35 wherein the particle is an HIV viral particle with a modified or heterologous Env protein.

52. The method of delivering a fusion protein to an individual administering a particle of claim 35.

53. A non-cellular particle that comprises a nucleotide sequence encoding a protein operably linked to regulatory elements derived from AAV, adenovirus or alphavirus wherein when said particle is a viral derived particle, said regulatory elements are derived from a different virus than said particle.

54. The particle of claim 53 wherein said particle is derived from a lentivirus.

55. The particle of claim 53 wherein said nucleotide sequence comprises a packaging signal which facilitates packaging of nucleic acid molecules by said particle.

56. A method of delivering and expressing DNA to cells of an individual that comprises administering to said individual a particle of claim 53.

57. A nucleotide sequence that encodes a protein operably linked to regulatory elements derived from AAV, adenovirus or alphavirus comprising a packaging signal which facilitates packaging of nucleic acid molecules by viral particles different from the viral particles from which said regulatory sequences have been derived.

L8 ANSWER 2 OF 18 USPTAFULL on STN

2005:49410 Compositions for and methods of treating and preventing sepsis

Weiner, David B., Merion Station, PA, UNITED STATES

Muthumani, Karupiah, Cherry Hill, NJ, UNITED STATES

US 2005042202 A1 20050224

APPLICATION: US 2004-491800 A1 20041007 (10)

WO 2002-US32084 20021007

PRIORITY: US 2001-327270P 20011005 (60)

DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods of inhibiting the immune response underlying sepsis, to methods of preventing sepsis, to

of treating sepsis and to pharmaceutical compositions useful in methods.

CLM What is claimed is:

1. A method of treating an individual who has been diagnosed as SIRS or sepsis comprising the step of administering to said individual therapeutically effective amount of an immuno-modulating pharmaceutical compositions comprising one or more of the components selected from the group consisting of: i) **Vpr** protein; ii) a function fragment of **Vpr** protein; iii) a nucleic acid encoding **Vpr** protein operably linked to regulatory elements; and iv) a nucleic acid encoding functional fragment of **Vpr** protein operably linked to regulatory elements.

2. The method of claim 1 wherein the individual is administered nucleic acid encoding **Vpr** protein or functional fragment thereof operably linked to regulatory elements.

3. The method of claim 2, wherein the nucleic acid is administered dose of 1 to 500 micrograms nucleic acid.

4. The method of claim 2, wherein the nucleic acid is administered dose of 25 to 250 micrograms nucleic acid.

5. The method of claim 2, wherein the nucleic acid is administered dose of about 100 micrograms nucleic acid.

6. The method of claim 2, wherein the nucleic acid encoding **Vpr** protein or functional fragment thereof operably linked to regulatory elements is contained in a plasmid.

7. The method of claim 2, wherein the nucleic acid encoding **Vpr** protein or functional fragment thereof operably linked to regulatory elements is contained in a viral vector.

8. The method of claim 7, wherein the viral vector is selected from the group consisting of a retroviral vector and an adenoviral vector

9. The method of claim 1, wherein the step of administering the immunomodulating pharmaceutical composition is repeated at least

10. The method of claim 9, wherein the step of administering the immunomodulating pharmaceutical composition is undertaken 1 to 6 day.

11. The method of claim 1, which additionally comprises at least step of administering to said individual a therapeutically effective amount of an anti-infective agent.

12. The method of claim 11, wherein the anti-infective agent is from the group consisting of: amikacin, tobramycin, netilmicin,

gentamicin, cephalosporin, ceftazidime, maxalactam, carbopenem, imipenem, aztreonam, ampicillin, penicillin, ureidopenicillin, augmentin, amphotericin, famvir and acyclovir.

13. The method of claim 11, wherein the step of administering the anti-infective agent is performed at the same time as the step of administering the immunomodulating pharmaceutical preparation.

14. The method of claim 1, which comprises the additional steps monitoring the concentration of pro-inflammatory cytokines and marker proteins/conditions in the blood plasma of the individual determining the need for additional doses of the immuno-modulating pharmaceutical composition and administering additional doses of immuno-modulating pharmaceutical composition.

15. The method of claim 14, wherein the blood plasma level of TNF is monitored and the need for additional doses of the immuno-modulating pharmaceutical composition is determined by a blood plasma level above about 25 pg/ml.

16. The method of claim 1, wherein the step of administering the immunomodulating pharmaceutical composition comprises continuous administration.

17. The method of claim 1 wherein the individual is administered a protein of a functional fragment thereof.

18. The method of claim 17, wherein the **Vpr** protein or functional fragment thereof is administered at 0.1 to 100 mg/kg body weight per day.

19. The method of claim 17, wherein the **Vpr** protein or functional fragment thereof is administered at 0.5 to 50 mg/kg body weight per day.

20. The method of claim 17, wherein the **Vpr** protein or functional fragment thereof is administered at 1.0 to 10 mg/kg body weight per day.

21. A method of preventing sepsis in an individual who has been identified as being at an elevated risk of contracting sepsis comprising the step of administering to said individual a prophylactically effective amount of an immuno-modulating pharmaceutical composition comprising one or more of the components selected from the group consisting of: i) **Vpr** protein; ii) a functional fragment of **Vpr** protein; iii) a nucleic acid encoding **Vpr** protein operably linked to regulatory elements; and iv) a nucleic acid encoding a functional fragment of **Vpr** protein operably linked to regulatory elements.

22-40. (Cancelled).

41. A pharmaceutical composition useful for preventing and treating sepsis.

sepsis, comprising an anti-infective agent and one or more of the components selected from the group consisting of: i) **Vpr** protein; ii) a function fragment of **Vpr** protein; iii) a nucleic acid encoding **Vpr** protein operably linked to regulatory elements; and iv) a nucleic acid encoding a functional fragment of **Vpr** protein operably linked to regulatory elements.

42. The pharmaceutical composition of claim 41, wherein the anti-infective agent is selected from the group consisting of: a tobramycin, netilmicin, gentamicin, cephalosporin, ceftazidime, maxalactam, carbopenem, imipenem, aztreonam, ampicillin, penicillin, ureidopenicillin, augmentin, amphotericin, famvir and acyclovir.

43. The pharmaceutical composition of claim 40, which additionally comprises at least one adjunctive agent in the treatment of SIRS

L8 ANSWER 3 OF 18 USPTAFULL on STN

2005:30708 Hiv-1 **vpr** interactions with mitochondrial apoptosis inducing factor and methods of using the same.

Weiner, David B., Merion Station, PA, UNITED STATES

Muthumani, Karupiah, Cherry Hill, NJ, UNITED STATES

US 2005026138 A1 20050203

APPLICATION: US 2004-478742 A1 20040802 (10)

WO 2002-US16731 20020528

PRIORITY: US 2001-293570P 20010525 (60)

DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Assays to identify **Vpr**/AIF interaction and translocation inhibitors are disclosed.

CLM What is claimed is:

1. A method of identifying compounds that inhibit HIV **Vpr** binding to AIF comprising a test assay that comprises the steps of: i) contacting a) HIV **Vpr** or a fragment of **Vpr** known to interact with AIF and b) AIF or a fragment of AIF which interacts with **Vpr** in the presence of c) a test compound and ii) comparing the level of HIV **Vpr** binding to AIF to the level of HIV **Vpr** binding to AIF in the absence of said compound.

2. The method of claim 1 wherein a) HIV **Vpr** and b) AIF or a fragment of AIF which interacts with **Vpr** are contacted in the presence of a test compound.

3. The method of claim 1 wherein a) HIV **Vpr** or a fragment of **Vpr** known to interact with AIF and b) AIF are contacted in the presence of c) a test compound.

4. The method of claim 1 wherein a) HIV **Vpr** and b) AIF are contacted in the presence of c) a test compound.

5. The method of claim 1 further comprising a positive control a that comprises the steps of: i) contacting a) HIV **Vpr** or a fra of **Vpr** known to interact with AIF and b) AIF or a fragment of AI which interacts with **Vpr** in the presence of c) anti-**Vpr antibodies** which competitively bind to **Vpr** with respect to AIF and/or anti **antibodies** which competitively bind to AIF with respect to **Vpr**.
6. The method of claim 1 wherein the concentration of test compo between 1 μM and 500 μM .
7. The method of claim 1 wherein the concentration of test compo between 10 μM to 100 μM .
8. The method of claim 1 wherein a series of test assays are per using a series of dilutions of test compounds.
9. A kit for performing the method of claim 1 comprising: a) a container comprising HIV **Vpr** or a fragment of **Vpr** known to inte with AIF; and, b) a second container comprising AIF or a fragma AIF which interacts with **Vpr** in the presence of c) a test compou and optionally, c) instructions for performing the test assay.
10. The kit of claim 9 further comprising a fourth container com anti-**Vpr antibodies** which competitively bind to **Vpr** with respec to AIF and/or anti-AIF **antibodies** which competitively bind to AI respect to **Vpr**.
11. A method of identifying compounds that inhibit HIV **Vpr**/AIF translocation comprising a test assay that comprises the steps o contacting, in the presence of a test compound, cells that compr **Vpr** or a fragment of **Vpr** known to interact with AIF and AIF or a fragment of AIF which interacts with **Vpr** in the presence and AI ii) comparing the level of **Vpr**/AIF in the nucleus to the level o **Vpr**/AIF in the nucleus in the absence of said test compound and/ comparing the level of **Vpr**/AIF in the cytoplasm to the level of **Vpr**/AIF in the cytoplasm in the absence of said test compound.
12. The method of claim 10 wherein the cells comprise a) HIV **Vp** b) AIF or a fragment of AIF which interacts with **Vpr**.
13. The method of claim 10 wherein the cells comprise a) HIV **Vp** fragment of **Vpr** known to interact with AIF and b) AIF.
14. The method of claim 10 wherein the cells comprise a) HIV **Vp** b) AIF.
15. The method of claim 1 wherein the concentration of test comp between 1 μM and 500 μM .

16. The method of claim 1 wherein the concentration of test comp between 10 μ M to 100 μ M.

17. The method of claim 1 wherein a series of test assays are pe using a series of dilutions of test compounds.

L8 ANSWER 4 OF 18 USPATFULL on STN

2005:471 **VPR** function and activity.

Weiner, David B., Merion, PA, United States

Levy, David Nathan, Philadelphia, PA, United States

Refaeli, Yosef, Philadelphia, PA, United States

The Trustees of the University of Pennsylvania, Philadelphia, PA, U States (U.S. corporation)The Wistar Institute, Philadelphia, PA, Un States (U.S. corporation)

US 6838236 B1 20050104

APPLICATION: US 1993-167608 19931215 (8)

DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Pharmaceutical compositions comprising the HIV protein **vpr** or n acid molecule encoding **vpr** are disclosed. Also disclosed are met of treating patients suffering from diseases characterized by hyperproliferating undifferentiated cells such as cancer by administering such compositions. Methods of identifying compound have anti-HIV activity are disclosed, in particular, methods of identifying compounds which modulate the activity of **vpr** and of identifying compounds which inhibit **vpr** binding to the HIV prot

CLM What is claimed is:

1. Isolated human immunodeficiency virus **Vpr** protein produced i eukaryotic cells.
2. A method of identifying whether or not an individual has been infected with human immunodeficiency virus comprising the steps contacting a test sample from said individual with isolated huma immunodeficiency virus **Vpr** protein produced in eukaryotic cells, b) detecting the presence of anti-**Vpr antibodies** bound to said **Vpr**, wherein the presence of anti-**Vpr antibodies** indicates that said individual has been infected with human immunodeficiency vi the absence of said anti-**Vpr antibodies** indicates that said individual has not been infected with human immunodeficiency vir
3. A kit for identifying whether or not an individual has been i with human immunodeficiency virus comprising a) a first containe comprising isolated human immunodeficiency virus **Vpr** protein pr in eukaryotic cells, and b) a second container which contains **antibodies** which specifically bind to **Vpr** protein produced in eukaryotic cells.
4. The isolated protein of claim 1 wherein said protein is immob to a solid phase support.

5. The isolated protein of claim 4, wherein said solid phase support is selected from the group consisting of: nitrocellulose paper, glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylase, natural and modified cellulose, polyacrylamide, agarose, and magnetite.
6. The isolated protein of claim 4, wherein said solid phase support is nitrocellulose paper or polystyrene.
7. The method of claim 2 wherein said test sample is selected from the group consisting of: blood, cerebral spinal fluid, amniotic fluid, lymph, semen or vaginal fluid.
8. The method of claim 2 wherein said test sample is blood.
9. The method of claim 2 wherein said **Vpr** protein is immobilized on solid phase support.
10. The method of claim 9 wherein said solid phase support is selected from the group consisting of: nitrocellulose paper, glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified cellulose, polyacrylamide, agarose, and magnetite.
11. The method of claim 9 wherein said solid phase support is nitrocellulose paper or polystyrene.
12. The method of claim 2 comprising the steps of: a) contacting test sample with **Vpr** protein that is immobilized to a solid phase support, and b) the presence of anti-**Vpr antibodies** bound to said **Vpr** is detected by i) adding anti-human **antibody antibodies** to said test sample and **Vpr** protein that is immobilized to a solid support; and ii) detecting said anti-human **antibody antibodies** to anti-**Vpr antibodies** that are bound to **Vpr** protein that is immobilized on said solid phase support.
13. The method of claim 12 wherein said anti-human **antibodies** are labelled.
14. The method of claim 2 further comprising the step of performing a positive control assay, said positive control assay comprising the steps of: a) contacting a positive control sample with **Vpr** protein produced in eukaryotic cells, wherein said positive control sample comprises positive control **antibodies** which are **antibodies** that bind to **V** produced in eukaryotic cells; and b) detecting the presence of said positive control **antibodies** bound to said **Vpr** produced in eukaryotic cells.
15. The method of claim 2 comprising the steps of: a) contacting test sample with **Vpr** protein that is immobilized to a solid phase support, and b) detecting the presence of anti-**Vpr antibodies** bound to said **Vpr** protein that is immobilized on said solid phase support.

to said **Vpr** by: i) washing said solid phase support; ii) adding said test sample and **Vpr** protein that is immobilized to said solid phase support, labelled **antibodies** that bind to human **antibody** region; iii) washing said solid phase support; iv) detecting said anti-human **antibodies** bound to said solid phase support.

16. The method of claim 15 wherein said anti-human **antibodies** are horse radish peroxidase labelled goat anti-human **antibodies**.

17. The kit of claim 3 wherein said **Vpr** protein is immobilized on a solid phase support.

18. The kit of claim 17 wherein said solid phase support is selected from the group consisting of: nitrocellulose paper, glass, polysilicone, polypropylene, polyethylene, dextran, nylon, amylases, natural or modified cellulose, polyacrylamide, agarose, and magnetite.

19. The kit of claim 17 wherein said solid phase support is nitrocellulose paper or polystyrene.

20. The kit of claim 3 further comprising a positive control which contains **antibodies** which specifically bind **Vpr** produced in eukaryotic cells.

21. An in vitro method of identifying individuals who have been exposed to the human immunodeficiency virus comprising the following steps: (i) preparing a test sample from said individual; (ii) admixing the sample of step (i) with isolated eukaryotically expressed human immunodeficiency virus **Vpr**; (iii) detecting the presence of anti **antibodies** bound to said **Vpr**; wherein the presence of said anti-**Vpr antibodies** indicates that said individual has been exposed to the human immunodeficiency virus.

22. The method of claim 21 wherein said test sample is selected from the group consisting of: blood, cerebral spinal fluid, amniotic fluid, lymph, semen or vaginal fluid.

23. The method of claim 21 wherein said test sample is blood.

24. The method of claim 21 wherein said **Vpr** protein is immobilized on a solid phase support.

25. The method of claim 24 wherein said solid phase support is selected from the group consisting of: nitrocellulose paper, glass, polysilicone, polypropylene, polyethylene, dextran, nylon, amylases, natural or modified cellulose, polyacrylamide, agarose, and magnetite.

26. The method of claim 24 wherein said solid phase support is nitrocellulose paper or polystyrene.

27. An in vitro method of identifying individuals who have been exposed to the human immunodeficiency virus comprising the following steps: (i) preparing a test sample from said individual; (ii) admixing the sample of step (i) with isolated eukaryotically expressed human immunodeficiency virus **Vpr** immobilized to a solid phase support; allowing **antibodies**, if present in the test sample, to bind to said **Vpr** to form an immune complex with said immobilized **Vpr**; (iv) detecting the presence of anti-**Vpr antibodies** bound to said **Vpr** by admixing a labeled anti-human secondary **antibody** with the immune complexes of step (iii); wherein the presence of said anti-**Vpr antibodies** indicates that said individual has been exposed to the human immunodeficiency virus.

28. The method of claim 27 wherein said anti-human secondary **antibody** is a goat anti-human **antibody** labeled with horseradish peroxidase.

29. A diagnostic kit for identifying individuals who have been exposed to the human immunodeficiency virus comprising the following components: (i) a container comprising isolated eukaryotically expressed human immunodeficiency virus **Vpr**; (ii) a container comprising a labeled anti-human secondary **antibody**; (iii) a container comprising **Vpr**-specific **antibodies**; (iv) a container comprising **antibodies** that do not bind to **Vpr**; and, (v) a container comprising detection reagents.

30. The kit of claim 29 wherein said **Vpr** is immobilized to a solid-phase support.

31. The kit of claim 30 wherein said solid phase support is selected from the group consisting of: nitrocellulose paper, glass, polysilicate, polypropylene, polyethylene, dextran, nylon, amylases, natural or modified cellulose, polyacrylamide, agarose, and magnetite.

32. The kit of claim 30 wherein said solid phase support is nitrocellulose paper or polystyrene.

L8 ANSWER 5 OF 18 USPTAFULL on STN

2004:328002 Compositions and methods for the abrogation of cellular proliferation utilizing the human immunodeficiency virus **Vpr** protein
Weiner, David B., Merion Station, PA, UNITED STATES

Levy, David N., Birmingham, AL, UNITED STATES

Refaeli, Yosef, Denver, CO, UNITED STATES

US 2004259827 A1 20041223

APPLICATION: US 2003-734024 A1 20031211 (10)

DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method of inhibiting proliferation of cells using **vpr** protein or nucleotide sequences that encode **vpr** are disclosed. Method of preventing lymphocyte activation using **vpr** protein or nucleotide

sequences that encode **vpr** are disclosed. Methods of treating an individual diagnosed with or suspected of suffering from autoimmune disease, diseases characterized by proliferating cells and graft host disease by administering **vpr** protein or a functional fragment thereof, or a nucleic acid molecule that comprises a nucleotide that encodes **vpr** protein or a functional fragment thereof are disclosed. Conjugated compositions for delivery of active agents nucleus of cells are disclosed.

CLM What is claimed is:

1. A method of inhibiting proliferation of cells which comprises step of: contacting cells with an amount of **vpr** protein or a functional fragment thereof effective to inhibit cell proliferation; or introducing into cells a nucleic acid molecule that comprises a nucleotide sequence that encodes **vpr** protein or a functional fragment thereof whereby said nucleotide sequence is expressed by said cells.
2. The method of claim 1 wherein said cells are differentiated.
3. The method of claim 1 wherein said cells are undifferentiated.
4. A method of preventing lymphocyte activation which comprises of: contacting a lymphocyte cell with an amount of **vpr** protein or a functional fragment thereof effective to prevent activation; or introducing into cells a nucleic acid molecule that comprises a nucleotide sequence that encodes **vpr** protein or a functional fragment thereof whereby said nucleotide sequence is expressed by said cells.
5. The method of claim 1 wherein said cells are T cells, B cells, monocytes.
6. A method of treating an individual diagnosed with or suspected of suffering from diseases characterized by hyperproliferating cells which comprises the step of administering to said individual an effective amount of a pharmaceutical composition comprising a) **vpr** protein or a functional fragment thereof, or a nucleic acid molecule that comprises a nucleotide sequence that encodes **vpr** protein or a functional fragment thereof; and b) pharmaceutically acceptable carrier.
7. A method of treating an individual diagnosed with or suspected of suffering from an autoimmune disease which comprises the step of administering to said individual an effective amount of a pharmaceutical composition comprising a) **vpr** protein or a functional fragment thereof, or a nucleic acid molecule that comprises a nucleotide that encodes **vpr** protein or a functional fragment thereof; and b) pharmaceutically acceptable carrier.
8. The method of claim 7 wherein said autoimmune disease is selected from the group consisting of: rheumatoid arthritis, multiple sclerosis, Sjogren's syndrome, sarcoidosis, insulin dependent diabetes mellitus, autoimmune thyroiditis, reactive arthritis, ankylosing spondylitis.

scleroderma, polymyositis, dermatomyositis, psoriasis, vasculiti Wegener's granulomatosis, Crohn's disease, ulcerative colitis, L Grave's disease, myasthenia gravis, autoimmune hemolytic anemia, autoimmune thrombocytopenia, asthma, cryoglobulinemia, primary b sclerosis and pernicious anemia.

9. A method of treating an individual who has a transplanted org tissue which comprises the step of administering to said individ effective amount of a pharmaceutical composition comprising a) protein or a functional fragment thereof, or a nucleic acid mole that comprises a nucleotide sequence that encodes **vpr** protein o functional fragment thereof; and b) pharmaceutically acceptable carrier.

10. A conjugated composition comprising: a first moiety which c isolated **vpr** or a rip-1-binding fragment thereof; and a second which comprises an active agent selected from the group consisti drug, a toxin, a nucleic acid molecule and a radioisotope; wher first moiety is covalently linked to said second moiety.

11. The conjugated composition of claim 10 wherein said first mo comprises **vpr**.

12. The conjugated composition of claim 10 wherein said second m comprises a nucleic acid molecule.

13. The conjugated composition of claim 10 wherein said second m comprises a DNA molecule.

L8 ANSWER 6 OF 18 USPATFULL on STN

2004:288529 Functional fragments of HIV-1 **Vpr** protein and methods of us the same.

Mahalingam, Sundarasamy, Birmingham, AL, United States

Ayyavoo, Velpandi, Monroeville, PA, United States

Patel, Mamata, Hoboken, NJ, United States

Kieber-Emmons, Thomas, Newtown Square, PA, United States

Weiner, David B., Merion Station, PA, United States

The Trustees of the University of Pennsylvania, Philadelphia, PA, U States (U.S. corporation)

US 6818627 B1 20041116

WO 9909412 19990225

APPLICATION: US 2000-485421 20001005 (9)

WO 1998-US16890 19980814

PRIORITY: US 1997-55754P 19970814 (60)

DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Conjugated compositions comprising a fragment of HIV-1 **Vpr** or a non-HIV-1 **Vpr** protein conjugated to a therapeutic compound and m of using the same to deliver therapeutic compounds to a cell's n

or for the preparation of drug delivery particles are disclosed. Functional fragments of HIV-1 **Vpr** and functional non-HIV-1 **Vpr** proteins, and pharmaceutical compositions comprising the same are disclosed. Methods of inhibiting cell proliferation and methods treating an individual who has a hyperproliferative disease are disclosed. Methods of identifying compounds that inhibit **Vpr** binding to the p6 domain of p55 or to p6 protein and kits for performing such methods are disclosed.

CLM

What is claimed is:

1. A conjugated composition comprising at least one a nuclear localization sequence fragment of HIV-1 **Vpr** protein (SEQ No: 1) consisting of amino acid sequence 17-36 and/or amino acid sequence of said HIV-1 **Vpr** protein conjugated to a therapeutic compound, wherein said therapeutic compound is a nucleic acid molecule.
2. The conjugated composition of claim 1, wherein said nucleic acid molecule is a DNA vaccine plasmid conjugated to said fragment of **Vpr** protein by covalent bonds.
3. The conjugated composition of claim 1, wherein said nucleic acid molecule is an antisense molecule.
4. The conjugated composition of claim 1, wherein said nucleic acid molecule is an antisense oligonucleotide.
5. A method of delivering a therapeutic compound to the nucleus of a cell comprising the step of: contacting said cell with a conjugated compound, wherein said conjugated compound comprises said therapeutic compound conjugated to at least one nuclear localization sequence fragment of HIV-1 **Vpr** protein (SEQ No: 1) consisting of amino acid sequence 17-36 and/or amino acid sequence 59-84 of said HIV-1 **Vpr** protein; wherein said therapeutic compound is a nucleic acid molecule and wherein said conjugated compound is taken up by said cell and localized to the nucleus of said cell.
6. The method of claim 5, wherein said nucleic acid molecule is a plasmid DNA molecule.
7. The method of claim 5, wherein said nucleic acid molecule is an antisense molecule.
8. The method of claim 5, wherein said nucleic acid molecule is an antisense oligonucleotide.
9. The method of claim 5, wherein said nucleic acid molecule is an antisense oligonucleotide.
10. A conjugated composition comprising a nuclear localization sequence fragment of HIV-1 **Vpr** protein (SEQ No: 1) comprising amino acid sequence 17-36 and/or amino acid sequence 59-84 of said HIV-1 **Vpr** protein.

protein conjugated to a therapeutic compound, wherein said fragm HIV-1 **Vpr** protein is less than 50 amino acids.

11. The conjugated composition of claim 10, wherein said fragmen HIV-1 **Vpr** protein further comprises a polycationic amino acid se

12. The conjugated composition of claim 10, wherein said therape compound is a DNA vaccine plasmid conjugated to said fragment of **Vpr** protein ionic bonds.

13. The conjugated composition of claim 10, wherein said fragmen HIV-1 **Vpr** protein further comprises a polycationic amino acid se and said therapeutic compound is a nucleic acid molecule conjuga said polycationic amino acid sequence by ionic bonds.

14. The conjugated composition of claim 10, wherein said therape compound is an antisense molecule.

15. The conjugated composition of claim 10, wherein said therape compound is an antisense oligonucleotide.

16. A method of delivering a therapeutic compound to the nucleus cell comprising the step of: contacting said cell with a conjuga compound, wherein said conjugated compound comprises said therap compound conjugated to a nuclear localization sequence fragment **Vpr** protein (SEQ No: 1) comprising amino acid sequence 17-36 an amino acid sequence 59-84 of said HIV-1 **Vpr** protein; wherein sa fragment of HIV-1 **Vpr** protein is less than 50 amino acids, and w said conjugated compound is taken up by said cell and localized nucleus of said cell.

17. The method of claim 16, wherein said therapeutic compound is molecule.

18. The method of claim 16, wherein said therapeutic compound is plasmid DNA molecule.

19. The method of claim 16, wherein said therapeutic compound is antisense molecule.

20. The method of claim 16, wherein said therapeutic compound is antisense oligonucleotide.

L8 ANSWER 7 OF 18 USPTAFULL on STN

2004:38115 Composition and methods of using hiv **vpr**.

Muthumani, Karrupiah, Upper Darby, PA, UNITED STATES

Weiner, David B., Merion Station, PA, UNITED STATES

US 2004028651 A1 20040212

APPLICATION: US 2002-311260 A1 20021213 (10)

AB Methods of delivering a desired polypeptide to an individual are disclosed. The methods comprise administering to the individual immunogenic vector comprising a nucleic acid encoding the desired polypeptide operably linked to regulatory elements in combination with one or more of **Vpr** protein, a functional fragment of **Vpr** protein, a nucleic acid encoding **Vpr** protein operably linked to regulatory elements, or a nucleic acid encoding fragment of **Vpr** protein operably linked to regulatory elements. Methods of inhibiting an undesirable immune response in an individual are disclosed. Methods for inhibiting the cellular proliferation of a tumor cell in an individual are disclosed.

CLM What is claimed is:

1. A method of delivering a desired polypeptide to an individual comprising administering to said individual: a) an immunogenic vector comprising a nucleic acid encoding the desired polypeptide operably linked to regulatory elements; and b) one or more of the components selected from the group consisting of: i) **Vpr** protein; ii) a functional fragment of **Vpr** protein; iii) a nucleic acid encoding **Vpr** protein operably linked to regulatory elements; and iv) a nucleic acid encoding a functional fragment of **Vpr** protein operably linked to regulatory elements.

2. The method of claim 1 wherein the individual is administered a nucleic acid encoding **Vpr** protein operably linked to regulatory elements.

3. The method of claim 2 wherein the nucleic acid encoding **Vpr** also encodes the desired polypeptide.

4. The method of claim 2 wherein a nucleic acid encoding **Vpr** protein and a nucleic acid encoding the desired polypeptide are administered to the individual in the same formulation.

5. The method of claim 4 wherein a nucleic acid encoding **Vpr** protein and a nucleic acid encoding the desired polypeptide are administered to the individual in separate formulations.

6. The method of claim 1 wherein the individual is administered **Vpr** protein.

7. The method of claim 6 wherein the **Vpr** protein and the nucleic acid encoding the desired polypeptide are administered in the same formulation.

8. The method of claim 6 wherein the **Vpr** protein and the nucleic acid encoding the desired polypeptide are administered in separate formulations.

9. The method of claim 1 wherein the desired polypeptide is a human polypeptide.
10. The method of claim 1 wherein the immunogenic vector is a viral vector.
11. The method of claim 10 wherein the viral vector is an adenoviral vector.
12. A composition comprising an immunogenic vector comprising a nucleic acid encoding the desired polypeptide operably linked to regulatory elements; and one or more of the components selected from the group consisting of: i) **Vpr** protein; ii) a functional fragment of **V** protein; iii) a nucleic acid encoding **Vpr** protein operably linked to regulatory elements; and iv) a nucleic acid encoding a functional fragment of **Vpr** protein operably linked to regulatory elements.
13. The composition of claim 12 comprising a nucleic acid encoding **Vpr** protein operably linked to regulatory elements.
14. The composition of claim 13 comprising a nucleic acid that encodes **Vpr** protein and the desired polypeptide.
15. The composition of claim 13 comprising **Vpr** protein.
16. The composition of claim 15 wherein the **Vpr** protein is incorporated within the immunogenic vector.
17. The composition of claim 15 wherein the immunogenic vector is a viral vector.
18. The composition of claim 17 wherein the viral vector is an adenoviral vector.
19. A method for inhibiting an undesirable immune response in an individual comprising administering to said individual in an amount sufficient to inhibit an undesirable immune response one or more components selected from the group consisting of: i) **Vpr** protein; ii) a functional fragment of **Vpr** protein; iii) a nucleic acid encoding **Vpr** protein operably linked to regulatory elements; and iv) a nucleic acid encoding a functional fragment of **Vpr** protein operably linked to regulatory elements.
20. The method of claim 19 wherein the individual is administered the nucleic acid encoding **Vpr** protein operably linked to regulatory elements.
21. The method of claim 19 wherein the individual is administered the **Vpr** protein.

22. The method of claim 19 wherein said individual has an autoimmune/inflammatory disease or condition.
22. The method of claim 19 wherein said individual is undergoing undergone a cell, tissue or organ transplant procedure.
23. The method of claim 19 wherein the undesirable immune response is septic shock.
24. The method of claim 23 wherein the component is administered prior to the undesirable immune response and the treatment is prophylactic.
25. The method of claim 23 wherein the component is administered to the undesirable immune response and the treatment is therapeutic.
26. The method of claim 19 wherein the undesirable immune response is toxic shock.
27. The method of claim 26 wherein the component is administered to the desirable immune response and the treatment is prophylactic.
28. The method of claim 26 wherein the component is administered to the undesirable immune response and the treatment is therapeutic.
29. A method for inhibiting cellular proliferation in a tumor-bearing individual comprising administering to said individual, in an amount sufficient to inhibit cellular proliferation, a recombinant adenovirus comprising a nucleic acid encoding Vpr protein operably linked to regulatory elements or a nucleic acid encoding an anti-tumor fragment of Vpr protein operably linked to regulatory elements.
30. The method of claim 29 wherein the recombinant adenovirus comprises a nucleic acid encoding Vpr protein operably linked to regulatory elements.
31. The method of claim 29 wherein the recombinant adenovirus comprises an anti-tumor fragment of Vpr protein operably linked to regulatory elements.
32. The method of claim 29 wherein the recombinant adenovirus is administered by intratumoral injection.

L8 ANSWER 8 OF 18 USPTAFULL on STN

2003:332329 Compositions and methods for the abrogation of cellular proliferation utilizing the human immunodeficiency virus VPR protein
Weiner, David B., Merion, PA, United States
Levy, David N., Birmingham, AL, United States
Refaeli, Yosef, Boston, MA, United States

Williams, William V., Havertown, PA, United States
Ayyavoo, Velpandi, Havertown, PA, United States
The Trustees of the University of Pennsylvania, Philadelphia, PA, U
States (U.S. corporation)
US 6667157 B1 20031223
WO 9608970 19960328
APPLICATION: US 1997-809186 19970624 (8)
WO 1995-US12344 19950921
DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method of inhibiting proliferation of cells using **vpr** protein o
nucleotide sequences that encode **vpr** are disclosed. Method of
preventing lymphocyte activation using **vpr** protein or nucleotid
sequences that encode **vpr** are disclosed. Methods of treating an
individual diagnosed with or suspected of suffering from autoimm
disease, diseases characterized by proliferating cells and graft
host disease by administering **vpr** protein or a functional fragme
thereof, or a nucleic acid molecule that comprises a nucleotide
that encodes **vpr** protein or a functional fragment thereof are
disclosed. Conjugated compositions for delivery of active agents
nucleus of cells are disclosed.

CLM What is claimed is:

1. A method of inhibiting proliferation of cells which comprises
steps a) obtaining isolated **Vpr** protein or a function fragment
thereof; and b) contacting cells with an amount of said **Vpr** pro
functional fragment thereof effective to inhibit cell proliferat
wherein said cells are T cells and/or B cells and/or monocytes.
2. The method of claim 1 which comprises the step of: contacting
with **Vpr** protein.
3. The method of claim 2 wherein said T cells and/or B cells and
monocytes are removed from an individual prior to being contacte
Vpr protein.
4. The method of claim 1 which comprises the step of: contacting
with a functional fragment of **Vpr** protein.
5. The method of claim 4 wherein said T cells and/or B cells-an
monocytes are removed from an individual prior to being contacte
said functional fragment of **Vpr** protein.
6. The method of claim 3 wherein said cells are T cells.
7. The method of claim 4 wherein said cells are monocytes.
8. The method of claim 3 wherein said cells are monocytes.
9. The method of claim 4 wherein said cells are T cells.

L8 ANSWER 9 OF 18 USPATFULL on STN
2003:294238 **VPR** function and activity.

Weiner, David B., Merion, PA, UNITED STATES
Levy, David Nathan, Philadelphia, PA, UNITED STATES
Refaeli, Yosef, Philadelphia, PA, UNITED STATES
US 2003207252 A1 20031106
APPLICATION: US 2001-935100 A1 20010822 (9)
DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Pharmaceutical compositions comprising the HIV protein **vpr** or a nucleic acid molecule encoding **vpr** are disclosed. Also disclosed are methods of treating patients suffering from diseases characterized by hyperproliferating undifferentiated cells such as cancer by administering such compositions. Methods of identifying compounds having anti-HIV activity are disclosed, in particular, methods of identifying compounds which modulate the activity of **vpr** and of identifying compounds which inhibit **vpr** binding to the HIV protein.

CLM What is claimed is:

1. A method of inducing undifferentiated cells to differentiate comprises the step of: contacting undifferentiated cells with a nucleic acid molecule encoding **vpr** protein or a functional fragment thereof effective to stimulate differentiation; or introducing into undifferentiated cells a nucleic acid molecule that comprises a nucleotide sequence that encodes **vpr** protein or a functional fragment thereof whereby said nucleotide sequence is expressed by said cells.

2. A pharmaceutical composition comprising a) **vpr** protein or a functional fragment thereof, or a nucleic acid molecule that comprises a nucleotide sequence that encodes **vpr** protein or a functional fragment thereof; and b) pharmaceutically acceptable carrier.

3. A method of treating an individual diagnosed with or suspected of suffering from diseases characterized by hyperproliferating undifferentiated cells which comprises the step of administering to said individual an effective amount of a pharmaceutical composition according to claim 2.

4. A pharmaceutical composition that comprises redifferentiated cells induced to redifferentiate by contacting tumor cells with **vpr** protein or introducing into tumor cells a nucleic acid molecule that comprises a nucleotide sequence that encodes **vpr** protein.

5. A method of treating an individual suffering from a disease associated with the loss or dysfunction of cells which comprises the step of implanting into said individual a pharmaceutical composition according to claim 4.

6. A method of identifying compounds which inhibit **vpr** from stimulating differentiation of undifferentiated cells which comprises the step of contacting undifferentiated cells with a compound and measuring the rate of differentiation of said cells.

the steps of a) contacting, in the presence of a test compound, undifferentiated cells with an amount of **vpr** protein sufficient to stimulate differentiation and b) comparing the differentiation that occurs with the differentiation that occurs when said undifferentiated cells are contacted with **vpr** protein in the absence of said test compound.

7. A kit for performing the method of identifying compounds which inhibit **vpr** from stimulating differentiation of undifferentiated cells of claim 6, said kit comprising a) a first container comprising undifferentiated cells, and b) a second container comprising **v** protein.

8. A method of identifying compounds that inhibit **vpr** protein binding to p55, p24, p15, p7 or p6 protein which comprises the steps of: contacting **vpr** protein or a fragment thereof and p55, p24, p15, p6 protein or a fragment thereof in the presence of a test compound, determining the level of binding between **vpr** protein and p55, p24, p15, p7 or p6 protein and c) comparing that level to the level of binding that occurs when **vpr** protein or a fragment thereof and p24, p15, p7 or p6 protein or a fragment thereof are contacted in the absence of a test compound.

9. A kit for performing the method of identifying compounds which inhibit **vpr** protein binding to p55, p24, p15, p7 or p6 protein of claim 8, said kit comprising: a) a first container comprising **vpr** protein or a fragment thereof and b) a second container comprising p24, p15, p7 or p6 protein or a fragment thereof.

10. A method of identifying compounds that inhibit p24 protein binding to p15 or p7 protein which comprises the steps of: a) contacting p24 protein or a fragment thereof and p15 or p7 protein or a fragment thereof in the presence of a test compound, b) determining the level of binding between p24 protein and p15 or p7 protein and c) comparing that level to the level of binding that occurs when p24 protein or a fragment thereof and p15 or p7 protein or a fragment thereof are contacted in the absence of a test compound.

11. A kit for performing the method of identifying compounds which inhibit p24 protein binding to p15 or p7 protein of claim 10, said kit comprising: a) a first container comprising p24 protein or a fragment thereof and b) a second container comprising p15 or p7 protein or a fragment thereof.

12. A method of identifying compounds which inhibit p24 aggregation which comprises the steps of: a) maintaining p24 protein under conditions which promote its aggregation in the presence of a test compound, b) determining the level of p24 aggregation and c) comparing that level to the level of aggregation that occurs when p24 protein is maintained under the same conditions in the absence of a test compound.

13. A kit for performing the method of identifying compounds which inhibit p24 aggregation of claim 12, said kit comprising a) a first container comprising p24 protein and b) a second container comprising p15 protein or MAb 1238.

14. Isolated **antibodies** which specifically bind to **vpr** protein produced in eukaryotic cells.

15. A method of identifying an individual exposed to HIV comprising steps of: a) contacting a sample with **antibodies** according to 14, and b) detecting whether said **antibodies** are bound to **vpr**.

16. A kit for identifying individuals exposed to HIV comprising first container comprising **antibodies** according to claim 14, and second container which contains **vpr** protein produced in eukaryotic cells.

17. Isolated **vpr** protein produced in eukaryotic cells.

18. A method of identifying an individual exposed to HIV comprising steps of: a) contacting a sample with **vpr** protein according to 17, and b) detecting whether said **vpr** is bound to **antibodies**.

19. A kit for identifying individuals exposed to HIV comprising first container comprising **vpr** protein according to claim 17, and a second container which contains **antibodies** which specifically bind to **vpr** protein produced in eukaryotic cells.

20. A method of enhancing retroviral propagation in cell culture comprising the step of: adding **vpr** protein in conjunction with infection of the cells by retrovirus; or introducing into a nucleic acid molecule that comprises a sequence that encodes **vpr** protein in conjunction with infecting said cells with a retrovirus.

21. A method of identifying compounds that inhibit **vpr** enhancement of retroviral replication comprising the steps of: a) infecting cells with a retrovirus in the presence of **vpr** protein and a test compound; b) infecting cells with a retrovirus in the presence of **vpr** protein, cells transformed with a nucleic acid molecule that comprises a nucleic acid sequence that encodes **vpr**, wherein the transformed cells produce **vpr** protein and c) comparing the amount of virus produced with the amount of virus produced by infecting cells with a retrovirus in the absence of a test compound.

22. A method of modifying macrophage cells comprising the step of contacting macrophage cells with **vpr** protein or introducing into macrophage cells a nucleic acid molecule that comprises a sequence that encodes **vpr** protein.

23. A method of treating individuals diagnosed with or suspected suffering from diseases characterized by undesirable activity of macrophage cells comprising the step of administering to such individuals, an effective amount of the pharmaceutical composition of claim 2.

24. Drug delivery particles comprising **vpr**, p24 and a non-HIV, cell-type specific envelope protein.

25. A method of delivering **vpr** to cells comprising administering drug delivery particle of claim 24.

26. A fusion compound comprising a biologically active portion and a **vpr** fragment which binds to p24.

27. Drug delivery particles comprising a fusion compound of claim 26 and a cell-type specific envelope protein.

28. A nucleic acid molecule that comprises a nucleotide sequence that encodes a fusion compound of claim 26.

29. An expression vector that comprises a nucleic acid molecule of claim 28.

30. A host cell that comprises an expression vector of claim 29.

31. A method of delivering a fusion compound to cells comprising administering a drug delivery particle of claim 27 wherein said particle comprises a biologically active portion linked to a **v** fragment which binds to p24

32. A pharmaceutical composition comprising a) **vpr**, an immunogenic fragment of **vpr** or anti-**vpr** antibodies; and b) a pharmaceutical acceptable carrier.

33. A method of treating an individual exposed to HIV by administering an immunogenic amount of **vpr**, an immunogenic fragment of **vpr** or an effective amount of anti-**vpr** antibodies.

=> d his

(FILE 'HOME' ENTERED AT 07:59:12 ON 04 APR 2005)

FILE 'USPATFULL' ENTERED AT 07:59:21 ON 04 APR 2005

L1 1 S US4808536/PN
L2 1 S US5001230/PN
L3 1 S US5874225/PN
E WEINER DAVID B/IN

L4 57 S E1 OR E3
 L5 33 S L4 AND (VPR OR VIRAL PROTEIN R)
 L6 33 S L5 AND (ANTIBOD?)
 L7 19 S L6 AND (ANTIBOD? (8W) VPR) OR (ANTIBOD? (8W) VIRAL PR
 L8 18 S L7 AND (ANTIBOD?/CLM OR VPR/CLM OR VIRAL PROTEIN R/CL

=> s (HIV or human immunodeficiency virus)
 36312 HIV
 436901 HUMAN
 20854 IMMUNODEFICIENCY
 85632 VIRUS
 14921 HUMAN IMMUNODEFICIENCY VIRUS
 (HUMAN(W) IMMUNODEFICIENCY(W) VIRUS)
 L9 38258 (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)

=> s l9 and (Vpr or viral protein R)
 1263 VPR
 75902 VIRAL
 196519 PROTEIN
 1047992 R
 39 VIRAL PROTEIN R
 (VIRAL(W) PROTEIN(W) R)
 L10 728 L9 AND (VPR OR VIRAL PROTEIN R)

=> s l10 and antibod?
 118424 ANTIBOD?
 L11 675 L10 AND ANTIBOD?

=> s l11 and ay<1994
 1977691 AY<1994
 L12 21 L11 AND AY<1994

=> d l12,cbib,1-21

L12 ANSWER 1 OF 21 USPATFULL on STN
 2005:471 **VPR** function and activity.
 Weiner, David B., Merion, PA, United States
 Levy, David Nathan, Philadelphia, PA, United States
 Refaeli, Yosef, Philadelphia, PA, United States
 The Trustees of the University of Pennsylvania, Philadelphia, PA, U
 States (U.S. corporation)The Wistar Institute, Philadelphia, PA, Un
 States (U.S. corporation)
 US 6838236 B1 20050104
 APPLICATION: US 1993-167608 19931215 (8) <-
 DOCUMENT TYPE: Utility; GRANTED.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 2 OF 21 USPATFULL on STN
 2000:109568 Antisense viruses and antisense-ribozyme viruses.
 Hu, Wen, Honolulu, HI, United States

Wang, Jie, Honolulu, HI, United States
 Inpax, Inc., Honolulu, HI, United States (U.S. corporation)
 US 6107062 20000822
 APPLICATION: US 1992-921104 19920730 (7) <-
 DOCUMENT TYPE: Utility; Granted.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 3 OF 21 USPATFULL on STN
 1999:24450 Identification of compounds that modulate HIV-1 vpr protein

Weiner, David B., Merion, PA, United States
 Levy, David Nathan, Philadelphia, PA, United States
 Trustees of The University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
 The Wistar Institute, Philadelphia, PA, United States (U.S. corporation)
 US 5874225 19990223
 APPLICATION: US 1993-19601 19930219 (8) <-
 DOCUMENT TYPE: Utility; Granted.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 4 OF 21 USPATFULL on STN
 1999:4039 Immunogenic peptides, **antibodies** and uses thereof relating to receptor binding.

Sodroski, Joseph G., Medford, MA, United States
 Haseltine, William A., Boston, MA, United States
 Olshevsky, Udy, Ramat-OAN, Israel
 Helseth, Eirik, Trondheim, Norway
 Furman, Craig D., Nashua, NH, United States
 Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corporation)
 US 5858366 19990112
 APPLICATION: US 1993-135312 19931012 (8) <-
 DOCUMENT TYPE: Utility; Granted.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 5 OF 21 USPATFULL on STN
 1998:159761 Method of intracellular binding of target molecules.

Marasco, Wayne A., Wellesley, MA, United States
 Haseltine, William A., Rockville, MD, United States
 Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corporation)
 US 5851829 19981222
 WO 9402610 19940203
 APPLICATION: US 1995-373190 19950330 (8) <-
 WO 1993-US6735 19930716 19950330 PCT 371 date 19950330 PCT 102(e)
 DOCUMENT TYPE: Utility; Granted.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 6 OF 21 USPATFULL on STN
 1998:122077 Immunogenic peptides, **antibodies** and uses thereof relating to receptor binding.

Sodroski, Joseph G., Medford, MA, United States

Haseltine, William A., Canbridge, MA, United States
Furman, Craig D., Nashua, NH, United States
Olshevsky, Udy, Remath-Oan, Israel
Helseth, Eirik, Trondheim, Norway
Wyatt, Richard, Tewksbury, MA, United States
Thali, Markus, Brookline, MA, United States
Dana-Farber Cancer Instistute, Boston, MA, United States (U.S. corp
US 5817316 19981006
APPLICATION: US 1992-858165 19920326 (7) <-
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 7 OF 21 USPATFULL on STN
1998:75745 DNA fragments obtained from a novel **human immunodeficiency virus** designated LAV_{MAL}.
Alizon, Marc, Paris, France
Sonigo, Pierre, Paris, France
Wain-Hobson, Simon, Montigny les Bretonneux, France
Montagnier, Luc, Le Plessis Robinson, France
Institut Pasteur, Paris, France (non-U.S. corporation)
US 5773602 19980630
APPLICATION: US 1993-154397 19931118 (8) <-
PRIORITY: FR 1986-401380 19860623
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 8 OF 21 USPATFULL on STN
1998:11867 Chimeric envelope proteins for viral targeting.
Weiner, David, Penn Wynn Hills, PA, United States
Williams, William, Havertown, PA, United States
Levy, David N., Philadelphia, PA, United States
The Wistar Institute of Anatomy & Biology, Philadelphia, PA, United
(U.S. corporation)The Trustees of the University of Pennsylvania,
Philadelphia, PA, United States (U.S. corporation)
US 5714316 19980203
APPLICATION: US 1993-147890 19931104 (8) <-
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 9 OF 21 USPATFULL on STN
97:107198 Composition containing a B epitope of the envelope glycoprote
retrovirus and a T epitope of another distinct protein of this retr
Girard, Marc, Paris, France
Gluckman, Jean-Claude, Paris, France
Bahraoui, El Mustapha, Marseille, France
Institut Pasteur, France (non-U.S. corporation)Universite Pierre et
Curie Paris VI, France (non-U.S. corporation)
US 5688914 19971118
APPLICATION: US 1993-150249 19931109 (8) <-
PRIORITY: FR 1989-110044 19890818

DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 10 OF 21 USPATFULL on STN

97:106928 Nucleotide sequences derived from the genome of retroviruses
HIV-1, HIV-2 and SIV type, and their uses in particular for the
amplification of the genomes of these retroviruses and for the in v
diagnosis of the disease due to these viruses.

Moncany, Maurice, Paris, France

Montagnier, Luc, Le Plessis-Robinson, France

Institut Pasteur, France (non-U.S. corporation) Institut National de
Sante et de la Recherche Medicale, France (non-U.S. corporation)

US 5688637 19971118

APPLICATION: US 1993-160465 19931202 (8)

<-

PRIORITY: FR 1989-7354 19890602

FR 1989-12371 19890920

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 11 OF 21 USPATFULL on STN

97:81129 Vectors containing **HIV** packaging sequences, packaging defectiv
HIV vectors, and uses thereof.

Sodroski, Joseph G., Medford, MA, United States

Haseltine, William A., Cambridge, MA, United States

Poznansky, Mark, Cambridge, MA, United States

Lever, Andrew, Pinner Middlesex, England

Gottlinger, Heinrich, Munich, Germany, Federal Republic of

Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corpo

US 5665577 19970909

APPLICATION: US 1993-152902 19931115 (8)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 12 OF 21 USPATFULL on STN

97:66033 YC1 gene.

Lu, Yichen, Wellesley, MA, United States

Haseltine, William A., Cambridge, MA, United States

Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corpo

US 5652144 19970729

APPLICATION: US 1992-973431 19921110 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 13 OF 21 USPATFULL on STN

97:3820 Genetic immunization.

Weiner, David B., Merion, PA, United States

Williams, William V., Havertown, PA, United States

Wang, Bin, Havertown, PA, United States

The Wistar Institute, Philadelphia, PA, United States (U.S. corpora

Trustees of the University of Pennsylvania, Philadelphia, PA, Unite

(U.S. corporation)
US 5593972 19970114
APPLICATION: US 1993-125012 19930921 (8) <-
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 14 OF 21 USPATFULL on STN
96:113834 Bacterial expression vectors containing DNA encoding secretio
signals of lipoproteins.
Stover, Charles K., Silver Spring, MD, United States
MedImmune, Inc., Gaithersburg, MD, United States (U.S. corporation)
US 5583038 19961210
APPLICATION: US 1992-977630 19921117 (7) <-
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 15 OF 21 USPATFULL on STN
96:111154 Multiple antigen peptide system having adjuvant properties, v
prepared therefrom and methods of use thereof.
Tam, James P., 607 S. Wilson Blvd., Nashville, TN, United States 3
US 5580563 19961203
WO 9322343 19931111
APPLICATION: US 1994-331489 19941228 (8) <-
WO 1993-US4179 19930503 19941228 PCT 371 date 19941228 PCT 102(e)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 16 OF 21 USPATFULL on STN
95:71261 Non-infectious **HIV** particles lacking long terminal repeats.
Haynes, Joel, Middleton, WI, United States
Klein, Michel H., Willowdale, Canada
Rovinski, Benjamin, Thornhill, Canada
Cao, Shi X., Etobicoke, Canada
Connaught Laboratories Limited, Willowdale, Canada (non-U.S. corpo
US 5439809 19950808
APPLICATION: US 1992-839751 19920615 (7) <-
PRIORITY: GB 1989-23123 19891013
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 17 OF 21 USPATFULL on STN
95:3945 Molecular clones of bovine immunodeficiency-like virus.
Gonda, Matthew A., Walkersville, MD, United States
The United States of America as represented by the Secretary of the
Department of Health and Human Services, Washington, DC, United Sta
(U.S. government)
US 5380830 19950110
APPLICATION: US 1992-980324 19921124 (7) <-
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 18 OF 21 USPATFULL on STN

94:44555 Drosophila cell lines expressing genes encoding MHC class I and B2-microglobulin and capable of assembling empty complexes and of making said cell lines.

Peterson, Per A., LaJolla, CA, United States

Jackson, Michael, Del Mar, CA, United States

Langlade-Demoyen, Pierre, Del Mar, CA, United States

Scripps Research Institute, LaJolla, CA, United States (U.S. corpor
US 5314813 19940524

APPLICATION: US 1992-841662 19920219 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 19 OF 21 USPATFULL on STN

93:52501 Characterization of replication competent human immunodeficiency 2 proviral clone HIV-2_{SBL/ISY}.

Franchini, Genoveffa, Washington, DC, United States

Wong-Staal, Flossie, San Diego, CA, United States

Gallo, Robert, Bethesda, MD, United States

United States of America, Washington, DC, United States (U.S. gover
US 5223423 19930629

APPLICATION: US 1989-331212 19890331 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 20 OF 21 USPATFULL on STN

93:31326 Gene expressing VPT protein and vectors expressing this protein

Haseltine, William A., Cambridge, MA, United States

Cohen, Eric, Brighton, MA, United States

Dana Farber Cancer Institute, Boston, MA, United States (U.S. corpor
US 5204258 19930420

APPLICATION: US 1989-360847 19890602 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 21 OF 21 USPATFULL on STN

92:46989 Multilayer solid phase immunoassay support and method of use.

Chan, Emerson W., Libertyville, IL, United States

Schulze, Werner, Waukegan, IL, United States

Robey, William G., Libertyville, IL, United States

Braun, Brian P., Gurnee, IL, United States

Daluga, Cynthia K., Lindenhurst, IL, United States

Kapsalis, Andreas A., Evanston, IL, United States

Knigge, Kevin M., Gurnee, IL, United States

Stephens, John E., Chicago, IL, United States

Stojak, II, Joseph J., Waukegan, IL, United States

Vallaris, David S., Grayslake, IL, United States

Durley, deceased, Benton A., late of Antioch, IL, United States by
W. Durley; executrix

Defreese, James D., Lindenhurst, IL, United States
Merkh, Carl W., Lindenhurst, IL, United States
Abbott Laboratories, Abbott Park, IL, United States (U.S. corporation)
US 5120662 19920609

APPLICATION: US 1990-532489 19900604 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d l12,cbib,ab,clm,10-21

L12 ANSWER 10 OF 21 USPATFULL on STN

97:106928 Nucleotide sequences derived from the genome of retroviruses
HIV-1, **HIV-2** and SIV type, and their uses in particular for the
amplification of the genomes of these retroviruses and for the in vivo
diagnosis of the disease due to these viruses.

Moncany, Maurice, Paris, France

Montagnier, Luc, Le Plessis-Robinson, France

Institut Pasteur, France (non-U.S. corporation) Institut National de
Sante et de la Recherche Medicale, France (non-U.S. corporation)

US 5688637 19971118

APPLICATION: US 1993-160465 19931202 (8)

<-

PRIORITY: FR 1989-7354 19890602

FR 1989-12371 19890920

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to nucleotidic sequences derived from genome
the **HIV-1** type virus, or from genomes of the **HIV-2** type virus,
the SIV type virus, and their applications, especially as
oligo-nucleotidic initiators of implementation of an in vitro
method for the diagnosis of the infection of an individual by a
the **HIV-1** and/or **HIV-2** type.

CLM What is claimed is:

1. An oligonucleotide primer, said primer having a nucleotide sequence
selected from the following group of nucleotides oriented in the
direction: nucleotides 636-653, 854-872, 1369-1388, and 2021-2024
gag gene of **HIV-1** Bru; nucleotides 900-881, 1385-1369, 1388-1369
2039-2021 of a nucleic acid sequence complementary to the gag gene
HIV-1 Bru; nucleotides 635-652, 864-888, 1403-1421, and 2055-2024
the gag gene of **HIV-1** Mal; nucleotides 916-897, 1419-1403, 1421
and 2073-2055 of a nucleic acid sequence complementary to the gag
of **HIV-1** Mal; nucleotides 636-653, 848-872, 1369-1388, and 2024
of the gag gene of **HIV-1** Eli; nucleotides 900-881, 1385-1369,
1388-1369, and 2042-2024 of a nucleic acid sequence complementary
gag gene of **HIV-1** Eli; nucleotides 859-876, 1160-1184, 1687-1703
2329-2349 of the gag gene of **HIV-2** ROD; nucleotides 1212-1193,
1703-1687, 1706-1687, and 2349-2329 of a nucleic acid sequence
complementary to the gag gene of **HIV-2** ROD; nucleotides 834-851
1124-1148, 1651-1670, and 2299-2318 of the gag gene of SIV-MAC;
nucleotides 1176-1157, 1667-1651, 1670-1651, and 2318-2299 of a

4/4/05

6860-6885, 7010-7032, 7306-7330, 7775-7800, 8787-8812, 7572-7598167-8185 of the env gene of HIV-1 Eli; and nucleotides 6885-687330-7306, 7800-7775, 8812-8787, and 8185-8167 of a nucleic acid sequence complementary to the env gene of HIV-1 Eli; nucleotide 9116-9136 of the nef1 gene of HIV-1 Bru; nucleotides 9136-91169503-9483 of a nucleic acid sequence complementary to the nef1 gene of HIV-1 Bru; nucleotides 9117-9137 of the nef1 gene of HIV-1 Mal; nucleotides 9137-9117 and 9505-9484 of a nucleic acid sequence complementary to the nef1 gene of HIV-1 Mal; nucleotides 9062-9082-9062 and 9449-9428 of a nucleic acid sequence complementary to the nef1 gene of HIV-1 Eli; nucleotides 9082-9062 and 9449-9428 of a nucleic acid sequence complementary to the nef1 gene of HIV-1 Eli; nucleotides 5073-5099 and 5383-5405 of the vif1 gene of HIV-1 Bru; nucleotides 5405-5383 and 5675-5653 of a nucleic acid sequence complementary to the vif1 gene of HIV-1 Bru; nucleotides 5068-5378-5400 of the vif1 gene of HIV-1 Mal; nucleotides 5400-53785670-5648 of a nucleic acid sequence complementary to the vif1 gene of HIV-1 Mal; and nucleotides 5037-5063 and 5347-5369 of the vif1 gene of HIV-1 Eli; nucleotides 5369-5347 and 5639-5617 of a nucleic acid sequence complementary to the vif1 gene of HIV-1 Eli; nucleotides 6081-6105 and 6240-6263 of the vpu gene of HIV-1 Bru; nucleotides 6343-6321 of a nucleic acid sequence complementary to the vpu gene of HIV-1 Bru; nucleotides 6076-6100 and 6238-6261 of the vpu gene of HIV-1 Mal; nucleotides 6338-6316 of a nucleic acid sequence complementary to the vpu gene of HIV-1 Mal; nucleotides 6045-6207-6230 of the vpu gene of SIV-MAC; and nucleotides 6307-6285 of a nucleic acid sequence complementary to the vpu gene of SIV-MAC.

2. An oligonucleotide primer selected from the group consisting of primers having the following nucleotide sequences from 5' to 3':
TGG CGC CCGAAC AGG GAC TGG CGC CTGAAC AGG GAC MMy2: GGC CAG GGG GAAAGAAAAA GGC CCG GCG GAAAGAAAAA MMy3: TGC CCA TACAAAATG TTT T CCA CAC TAT ATG TTT TA MMy4: TGC ATG GCT GCT TGA TG TGC ATA GCT TG MMy4B: CTT TGC ATG GCT GCT TGA TG CTC TGC ATA GCT GCT TGC TG CAT CAAGCA GCC ATG CAAAG CAC CAG GCA GCT ATG CAG AG MMy28: AGG GGAAAT GTG G AGG GCT GTT GGA AGT GTG G MMy28a: CCA CAT TTC CAG T CCA CAT TTC CAG CAG CCC T CCA CAT TTC CAG CAC CCC T MMy18: G TGGAAC AAG CCC CAG MMy19: TCC ATT TCT TGC TCT CCT CTG T MMy29: T CAG GAA TGG ATG GCC CAA TAAAGC CAG GAA TGG ATG GAC CAA MMy29a: CAT CCA TTC CTG GCT TTA TTG GTC CAT CCA TTC CTG GCT TTA MMy30: GTC AAT GAC ATA CAGAA TGG ACT GTC AAT GAT ATA CAGAA MMy30a: TTC TCA TTG ACA GTC CA TTC TGT ATG TCA TTG ACT GTC CA MMy31: CAT GG CAG CAC ACAAAG G MMy31a: CCT TTG TGT GCT GGT ACC CAT G MMy32: TG GGT GAA GGG GCA GT TGG AAA GGT GAAGGA GCA GT MMy32a: ACT GCC CC CCT TTC CA ACT GCC CCT TCT CCT TTC CA ACT GCC CCT TCC CCT TTC MMy12: AGA GAC TCT TGC GGG CGC GTG MMy13: ATA TAC TTA GAAAAG GAA MMy13a: CCT TCT TCC TTT TCTAAG TAT AT MMy14: AGC TGA GAC AGC AGG CCA MMy20: TAT GGA GGA GGAAAAGAG ATG GAT AGT MMy21: TAG CAC TTA TTG CTT T MMy21a: AAA GCA AGG GAAATA AGT GCT A MMy22: CCC TTG TT ATG CCA GTA T MMy23: ATG TCA GAT CCC AGG GAG A MMy24: CCT GGA GG GGA GGA GGA MMy5: CCA ATT CCC ATA CAT TAT TGT GCC CC MMy5a: GGG

TAATGT ATG GGA ATT GG MMy6: AAT GGC AGT CTA GCA GAA GAA GA MMy7:
AOG AGG GGA CCC AGAAAT T MMy7a: AAT TTC TGG GTC CCC TCC TGA GGA
GTG CTT CCT GCT GCT CCC AAG AAC CC MMy8a: GGG TTC TTG GGA GCA GC
AGC AC MMy9: ATG GGT GGC AAG TGG TCAAAAAGT AG ATG GGT GGCAAAATGG
TCAAAAAGT AG MMy9a: CTA CTT TTT GAC CAC TTG CCA CCC AT MMy89: TT
CTT TTC TTG CTG G MMy10: AAAAGAAAAGGG GGG ACT GGA MMy10a: TCC AG
CCC TTT TCT TTT MMy11: AAA GTC CCC AGC GGAAAG TCC C MMy15: GAT T
GGAAAA CAG ATG GCA GGT GAT MMy16: GCAGAC CAACTA ATT CAT CTG TA M
TAC AGA TGA ATT AGT TGG TCT GC MMy17: CTT AAG CTC CTC TAAAAG CTC
MMy25: GTA AGT AGT ACA TGTAAT GCA ACC T MMy26: AGC AGA AGA CAG T
CCATGA GAG MMy27: ACT ACA GAT CAT CAATAT CCC AA.

3. A method for amplifying nucleic acids of viruses of the **HIV-1**, **HIV-2**, and SIV type in a biological sample, said method comprising:
a) extracting said nucleic acid from said biological sample; b) treating said nucleic acid with a reverse transcriptase if said nucleic acid is RNA; and c) performing an amplification cycle comprising the following steps: denaturing the nucleic acid to be detected to form single-stranded nucleic acids, hybridizing each of said nucleic acid single strands with at least one primer according to any one of claims 1 and 2, by placing said single strands in contact with at least one of said primers, and amplifying said nucleic acid strands by elongation of said primers along the strands to which they are hybridized in the presence of a polymerase, dATP, dGTP, dCTP and dTTP, said cycle being repeated about 30 to about 40 times.

4. The method of claim 3 wherein the step of denaturing the nucleic acid is carried out in the presence of said primer.

5. A method of in vitro diagnosis of infection of a mammal by a virus selected from the group consisting of **HIV-1**, **HIV-2**, and SIV, said method comprising detecting nucleic acid of said virus by:
a) obtaining a biological sample from said mammal, wherein said biological sample comprises nucleic acid; b) extracting nucleic acid of said virus from said biological sample and, if said nucleic acid is RNA, treating said nucleic acid with a reverse transcriptase to produce a double-stranded nucleic acid comprising said nucleic acid and its complementary strand; c) performing an amplification cycle comprising the following steps: denaturing the double-stranded nucleic acid to be detected to form single-stranded nucleic acids, hybridizing each of said nucleic acid single strands with at least one primer according to any one of claims 1 and 2, by placing said single strand in contact with said primer under hybridization conditions, and amplifying said nucleic acid single strands by elongation of said primers along the strands to which they are hybridized in the presence of a polymerase, dATP, dGTP, dCTP and dTTP, said cycle being repeated about 10 to about 60 times; d) detecting the nucleic acid of said virus and e) correlating the presence of said nucleic acid of said virus with infection by said virus.

6. The diagnostic method of claim 5, wherein the hybridization step is carried out in the presence of said primer.

nucleotides of the nucleic acid of said virus, and said second p complementary to a region of nucleotides of the strand of DNA complementary to said nucleic acid of said virus, wherein said r of nucleotides are separated by about 50 to about 10,000 base pa said complementary strands are incorporated into one double-str nucleic acid; b) reagents for amplifying said nucleic acid; and least one detectably labelled probe capable of hybridizing with amplified nucleotide sequence to be detected.

14. An oligonucleotide primer couple for the amplification accor any one of claims 3 and 5, said primer couple selected from the consisting of MMy4Ba-MMy28a, MMy26-MMy5a, MMy8a-MMy89, MMy89a-M MMy25-MMy27, MMy26-MMy27, MMy28-MMy29a, MMy29-MM30a, MMy30-MMy3 MMy31-MMy32a.

L12 ANSWER 11 OF 21 USPATFULL on STN

97:81129 Vectors containing **HIV** packaging sequences, packaging defectiv **HIV** vectors, and uses thereof.

Sodroski, Joseph G., Medford, MA, United States

Haseltine, William A., Cambridge, MA, United States

Poznansky, Mark, Cambridge, MA, United States

Lever, Andrew, Pinner Middlesex, England

Gottlinger, Heinrich, Munich, Germany, Federal Republic of

Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corpo
US 5665577 19970909

APPLICATION: US 1993-152902 19931115 (8)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Packaging defective and packaging proficient **HIV** vectors are disclosed. These vectors can be used to establish **HIV** packaging defective cell lines, and to package desired genes. These cell l be used in developing a vaccine, **HIV antibodies** and as part of system for gene transfer. The packaging proficient vector can be target **HIV** target cells.

CLM What is claimed is:

1. An **HIV** vector comprising: (a) a DNA segment from an **HIV** geno wherein the DNA segment comprises the **HIV** gag, pol and env gene wherein said **HIV** vector lacks the **HIV** packaging sequence necessa to package **HIV** RNA into virions; wherein said **HIV** packaging seq is the nucleotide sequence located between the 5' major splice d site and the initiation codon of the gag gene on the **HIV** genome (b) a promoter operably linked to the DNA segment from an **HIV** g of (a); wherein the **HIV** vector, when introduced into a eukaryoti cell, express **HIV** gag, pol and env proteins to form **HIV** virions do not contain sufficient **HIV** RNA to result in a replication com **HIV** virion.

2. The **HIV** vector claim 1, wherein the promoter is an **HIV** LTR.

3. The **HIV** vector of claim 1, wherein the promoter functions to express genes preferentially in specific cell types.
4. The **HIV** vector claim 3, wherein the promoter is a CMV promote
5. The **HIV** vector of claim 1, wherein the **HIV** packaging sequenc a nucleotide sequence located from the 5' major splice donor sit about 5 bases upstream of the gag gene initiation codon.
6. The **HIV** vector of claim 1, wherein the **HIV** packaging sequenc a nucleotide sequence located from about 9 bases downstream of t major splice donor site to about 14 bases upstream of the gag ge initiation codon.
7. The **HIV** vector of claim 1, wherein the **HIV** packaging sequenc the sequence AAAAATTTTGACTAGCGGA.
8. The **HIV** vector of claim 1, wherein the **HIV** genome is an **HIV**-
9. Thee **HIV** vector of claim 7, wherein the **HIV** genome is an **HIV** genome.
10. The **HIV** vector of claim 8, wherein the promoter is an **HIV**-1
11. The **HIV** vector of claim 9, wherein the promoter is an **HIV**-1
12. At least two **HIV** vectors, wherein each of the at least two vectors has (a) a DNA segment encoding a gag or an env gene from **HIV** genome but not both, wherein one of the at least two **HIV** ve or an additional **HIV** vector has a DNA segment encoding a pol gen an **HIV** genome, wherein each of the **HIV** vectors lacks the **HIV** packaging sequence necessary to package **HIV** RNA into virions; w said **HIV** packaging sequence is the nucleotide sequence located b the 5' major splice donor site and the initiation codon of the g on the **HIV** genome; (b) a promoter operably linked to each of the segments from an **HIV** genome of (a); and (c) a polyadenylation se located downstream of each of the DNA segments from an **HIV** geno (a); wherein the polyadenylation sequence does not comprise a fu LTR sequence; wherein the vectors, when introduced into a eukary host cell, express in combination the gag, pol and env proteins **HIV** virions that do not contain sufficient **HIV** RNA to result in replication competent **HIV** virion.
13. Two **HIV** vectors, wherein each vector has inserted therein: (exactly one of two of any of three DNA segments from an **HIV** gen wherein the three DNA segments are selected from the group consi the **HIV** gag, pol and env genes; wherein each of the two vectors the **HIV** packaging sequence necessary to package **HIV** RNA into virions; wherein said **HIV** packaging sequence is the nucleotide sequence located between the 5' major splice donor site and the

initiation codon of the gag gene on the **HIV** genome; (b) a promoter operably linked to each of the DNA segments from an **HIV** genome and (c) a polyadenylation sequence located downstream of each of the segments from an **HIV** genome of (a); wherein the polyadenylation sequence does not comprise a functional LTR sequence; wherein the vectors, when introduced into a eukaryotic host cell, express in combination the gag, pol and env proteins to form **HIV** virions that do not contain sufficient **HIV** RNA to result in a replication competent **HIV** virion.

14. The two **HIV** vectors of claim 13, wherein either or both vectors further comprise at least one **HIV** regulatory gene which expresses a functional **HIV** regulatory protein in said eukaryotic host cell.

15. The two **HIV** vectors of claim 14, wherein said **HIV** regulatory gene is selected from the group consisting of tat, rev, vif, vpr, vpu, and vpx.

16. The two **HIV** vectors of claim 13, wherein the **HIV** vector containing the **HIV** env gene does not also contain the gag gene.

17. The two **HIV** vectors of claim 13, wherein the promoter of (b) is an **HIV** LTR.

18. The two **HIV** vectors of claim 13, wherein the **HIV** packaging sequence is a nucleotide sequence located from the 5' major splice site to about 5 bases upstream of the gag initiation codon.

19. The two **HIV** vectors of claim 13, wherein the **HIV** genome is selected from the group consisting of **HIV**-1 and **HIV**-2.

20. The two **HIV** vectors of claim 13, wherein the **HIV** genome is the **HIV**-1 genome.

21. The two **HIV** vectors of claim 13, wherein the **HIV** genome is the **HIV**-2 genome.

22. The two **HIV** vectors of claim 13, wherein the first of the two **HIV** vectors contains both the **HIV** gag and the **HIV** pol genes.

23. The two **HIV** vectors of claim 22, wherein the second of the two **HIV** vectors contains the env gene.

24. The two **HIV** vectors of claim 22, wherein the promoter for the first of the two **HIV** vectors is an **HIV** LTR.

25. The two **HIV** vectors of claim 23, wherein the promoter for the second of the two **HIV** vectors is an **HIV** LTR.

26. The two **HIV** vectors of claim 23, wherein the polyadenylation

sequence is the SV40 polyadenylation sequence.

27. The two **HIV** vectors of claim 22, wherein the polyadenylation sequence for the first of the two **HIV** vectors is the SV40 polyadenylation sequence.

28. The two **HIV** vectors of claim 23, wherein the polyadenylation sequence for the second of the two **HIV** vectors is the SV40 polyadenylation sequence.

29. The two **HIV** vectors of claim 28, wherein the second of the **HIV** vectors further comprises an **HIV** rev gene which expresses a functional **HIV** rev protein in said eukaryotic host cell.

30. The two **HIV** vectors of claim 13 wherein each of the two **HIV** vectors further comprises an **HIV** RRE sequence.

31. Three vectors, wherein the first two vectors consist of the **HIV** vectors of claim 13, and the third vector is a retroviral vector which comprises: (i) a gene of interest, wherein said gene is heterologous to an **HIV** genome; (ii) a promoter operably linked to the gene of (i); (iii) an **HIV** packaging sequence necessary to package **HIV** RNA into **HIV** virions; and (iv) single **HIV** LTRs flanking the sequences of (i), (ii) and (iii), wherein the **HIV** LTRs are the 5' **HIV** LTR and the 3' **HIV** LTR which permit reverse transcription and integration of the third vector in a eukaryotic host cell; where the first two **HIV** vectors, when introduced into a eukaryotic host cell, express in combination the **HIV** gag, pol and env proteins such that when the third vector is also introduced into said host cell, the gag, pol and env proteins will package the third vector into infectious **HIV** vector virions.

32. The three vectors of claim 31, wherein the gene of (i) further comprises a polyadenylation sequence located downstream of said gene.

33. The three vectors of claim 31, wherein the third vector further comprises a second gene heterologous to an **HIV** genome.

34. The three vectors of claim 31, wherein the **HIV** packaging sequence of (iii), present in the third vector, is the nucleotide sequence located between the 5' major splice donor site and up to at most nucleotide position 385 located in the 5' portion of the gag gene on the **HIV**-1 genome.

35. The three vectors of claim 31, wherein the **HIV** packaging sequence of (iii), present in the third vector, is the nucleotide sequence located between the 5' major splice donor site and about nucleotide position 338 to 385 located in the 5' portion of the gag gene on the **HIV**-1 genome.

36. The three vectors of claim 31, wherein the **HIV** packaging sequence of (iii), present in the third vector, is the nucleotide sequence located between the 5' major splice donor site and about nucleotide position 350 to 381 located in the 5' portion of the gag gene on **HIV-1** genome.

37. The three vectors of claim 31, wherein the **HIV** packaging sequence of (iii), present in the third vector, is the nucleotide sequence located between the 5' major splice donor site and a **Bal I** restriction site at the 3' end of the gag gene of the HXBc2 strain of **HIV-1**.

38. The three vectors of claim 31, wherein the promoter of (ii) is a viral promoter.

39. The three vectors of claim 38, wherein the viral promoter is the **HIV** promoter.

40. The three vectors of claim 31, wherein the gene of (i) encodes a trans-dominant inhibitor protein, an antisense RNA, a catalytic soluble CD4 protein.

41. The three vectors of claim 31, wherein the promoter of (ii) is the 5' **HIV** LTR of (iv).

42. The three vectors of claim 31, wherein the promoter of (ii) is a promoter heterologous to an **HIV** genome.

43. Two **HIV** vectors wherein (a) one **HIV** vector, referred to as first vector, contains a DNA segment from an **HIV** genome consisting of the **HIV** gag gene or the **HIV** gag-pol genes, wherein said first vector does not contain a DNA segment containing the **HIV** env gene, wherein said first vector can optionally contain a DNA segment from an **HIV** genome consisting of the **HIV** pol gene, (b) the other **HIV** vector referred to as said second vector, contains a DNA segment from an **HIV** genome consisting of the **HIV** env gene, wherein said second vector does not contain a DNA segment containing the **HIV** gag gene, wherein said second vector can optionally contain a DNA segment from an **HIV** genome consisting of the **HIV** pol gene, (c) wherein each of the **HIV** vectors lacks the **HIV** packaging sequence necessary to package **HIV** RNA into virions; wherein said **HIV** packaging sequence is the nucleotide sequence located between the 5' major splice donor site and the initiation codon of the gag gene on the **HIV** genome; (d) a promoter operably linked to each of the DNA segments from an **HIV** genome of (a) and (b); and (e) a polyadenylation sequence located downstream of the DNA segments from an **HIV** genome of (a) and (b); wherein the two **HIV** vectors, when introduced into a eukaryotic host cell, express in combination the gag, pol and env proteins to form virions that do not contain sufficient **HIV** RNA to result in a replication competent **HIV** virion.

44. The two **HIV** vectors of claim 43, wherein either or both **HIV** vectors further comprise at least one **HIV** regulatory gene which expresses a functional **HIV** regulatory protein in said eukaryotic cell.

45. The two **HIV** vectors of claim 44, wherein said **HIV** regulator gene is selected from the group consisting of tat, rev, vpu, **vp** vif.

46. The two **HIV** vectors of claim 43 wherein each of the two **HIV** vectors further comprises an **HIV** RRE sequence.

47. Three vectors, wherein the first two vectors consist of the **HIV** vectors of claim 43, and the third vector is a retroviral vector which comprises: (i) a gene of interest, wherein said gene is heterologous to an **HIV** genome; (ii) a promoter operably linked to gene of (i); (iii) an **HIV** packaging sequence necessary to package **HIV** RNA into virions; and (iv) single **HIV** LTRs flanking the sequences of (i), (ii) and (iii), wherein the **HIV** LTRs are the **HIV** LTR and the 3' **HIV** LTR which permit reverse transcription and integration of the third vector in a eukaryotic host cell; where first two **HIV** vectors, when introduced into a eukaryotic host cell express in combination the **HIV** gag, pol and env proteins such that when the third vector is also introduced into said host cell, the gag, pol and env proteins will package the third vector into infectious **HIV** vector virions.

48. The three vectors of claim 47, wherein the gene of (i) further comprises a polyadenylation sequence located downstream of said

49. The three vectors of claim 47, wherein the third vector further comprises a second gene heterologous to an **HIV** genome.

50. The three vectors of claim 47, wherein the promoter of (ii) is a viral promoter.

51. The three vectors of claim 50, wherein the viral promoter is the viral promoter.

52. The three vectors of claim 47, wherein the gene of (i) encodes a trans-dominant inhibitor protein, an antisense RNA, a catalytic soluble CD4 protein.

53. Four vectors, wherein the first three vectors consist of the vectors of claim 47, and the fourth vector is an **HIV** vector which contains: (f) a DNA segment from an **HIV** genome consisting of at least one **HIV** regulatory gene, wherein the fourth vector lacks the **HIV** packaging sequences necessary to package **HIV** RNA into virions; said **HIV** packaging sequence is the nucleotide sequence located between

the 51 major splice donor site and the initiation codon of the g on the **HIV** genome; (g) a promoter operably linked to the DNA seg from the **HIV** genome of (f), and (h) a polyadenylation sequence 1 downstream of the DNA segments from the **HIV** genome of (g), wher polyadenylation sequence does not comprise a functional LTR sequ

54. The four vectors of claim 53, wherein the fourth vector cont **HIV** vpu gene and does not contain the **HIV** gag and env genes.

55. A method of producing an **HIV** packaging cell line which compr transforming an established cell line with the vectors of claim

56. A method of producing an **HIV** packaging cell line which compr transforming an established cell line with the vector of claim 1

57. A method of producing an **HIV** packaging cell line which compr transforming an established cell line with the vectors of claim

58. A method of producing an **HIV** packaging cell line which compr transforming an established cell line with the vectors of claim

59. The method of claim 55, wherein the established cell line is mammalian cell line.

60. The method of claim 56, wherein the established cell line is mammalian cell line.

61. The method of claim 57, wherein the established cell line is mammalian cell line.

62. The method of claim 58, wherein the established cell line is mammalian cell line.

63. An **HIV** packaging cell line which comprises an established ce line transformed by the vectors of claim 12.

64. An **HIV** packaging cell line which comprises an established ce line transformed by the vector of claim 1.

65. An **HIV** packaging cell line which comprises an established ce line transformed by the vectors of claim 13.

66. An **HIV** packaging cell line which comprises an established ce line transformed by the vectors of claim 43.

67. A method of transferring a gene of interest to a mammalian c comprising: (a) transfecting a eukaryotic host cell with the thr vectors of claim 31; (b) culturing the transfected host cell of collecting the packaged virions produced; (c) administering the of (b) to a mammalian cell to allow infection of the mammalian c

transfer of the gene of interest.

68. A method of transferring a gene of interest to a mammalian cell comprising: (a) transfecting a eukaryotic host cell with the vectors of claim 47; (b) culturing the transfected host cell of collecting the packaged virions produced; (c) administering the of (b) to a mammalian cell to allow infection of the mammalian cell transfer of the gene of interest.

69. The method of claim 67, wherein the mammalian cell is located in vitro.

70. The method of claim 68, wherein the mammalian cell is located in vitro.

71. The method of claim 67, wherein the mammalian cell is located in vivo.

72. The method of claim 68, wherein the mammalian cell is located in vivo.

L12 ANSWER 12 OF 21 USPTAFULL on STN

97:66033 YC1 gene.

Lu, Yichen, Wellesley, MA, United States

Haseltine, William A., Cambridge, MA, United States

Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corporation)
US 5652144 19970729

APPLICATION: US 1992-973431 19921110 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Isolated and purified YC1 genes and proteins are disclosed. The YC1 gene binds to a site in the HIV-LTR, the NRE-1 site, and can inhibit expression of a gene operably linked to the HIV-1 LTR. The use of the protein and gene are discussed. Repressible and inducible expression systems using the YC1 gene are also disclosed.

CLM What is claimed is:

1. An isolated and purified nucleic acid segment having SEQ ID NO:1 a portion of said segment wherein said segment or said portion the encodes a protein that binds to a HIV LTR NRE-1 site and inhibits expression of a gene operably linked to said HIV LTR NRE-1 site

2. An RNA molecule encoded by the nucleic acid segment in claim 1

3. A vector comprising a promoter operably linked to the nucleic acid segment of claim 1.

4. An isolated and purified nucleic acid sequence having a segment having SEQ ID NO:2 or a portion of said segment, wherein said segment or said portion encodes a protein that binds to a HIV LTR NRE-1 site

inhibits expression of a gene operably linked to said **HIV** LTR N site, wherein said segment or said portion is operably linked to promoter.

L12 ANSWER 13 OF 21 USPATFULL on STN

97:3820 Genetic immunization.

Weiner, David B., Merion, PA, United States

Williams, William V., Havertown, PA, United States

Wang, Bin, Havertown, PA, United States

The Wistar Institute, Philadelphia, PA, United States (U.S. corpora
Trustees of the University of Pennsylvania, Philadelphia, PA, Unite
(U.S. corporation)

US 5593972 19970114

APPLICATION: US 1993-125012 19930921 (8)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of prophylactic and therapeutic immunization of an indiv against pathogen infection, diseases associated with hyperprolif cells and autoimmune diseases are disclosed. The methods compris steps of administering to cells of an individual, a nucleic acid molecule that comprises a nucleotide sequence that encodes a pro which comprises at least one epitope that is identical or substa similar to an epitope of a pathogen antigen, a hyperproliferativ associated protein or a protein associated with autoimmune disea respectively. In each case, nucleotide sequence is operably link regulatory sequences to enable expression in the cells. The nucl molecule is free of viral particles and capable of being express said cells. The cells may be contacted cells with a cell stimula agent. Methods of prophylactically and therapeutically immunizin individual against **HIV** are disclosed. Pharmaceutical composition kits for practicing methods of the present invention are disclos

CLM What is claimed is:

1. A method of immunizing an individual comprising: injecting in skeletal muscle tissue of said individual at a site on said indi body, bupivacaine and a DNA molecule that comprises a DNA sequen encodes an antigen from a pathogen, said DNA sequence operative to regulatory sequences which control the expression of said DNA sequence; wherein said DNA molecule is taken up by cells in said skeletal muscle tissue, said DNA sequence is expressed in said c an immune response is generated against said antigen.

2. The method of claim 1 wherein said pathogen is an intracellul pathogen.

3. The method of claim 1 wherein said pathogen is a virus select the group consisting of: **human immunodeficiency virus, HIV**; human T cell leukemia virus, HTLV; influenza virus; hepatitis A hepatitis B virus; hepatitis C virus; human papilloma virus, HPV simplex 1 virus, HSV1; Herpes simplex 2 virus, HSV2; Cytomegalov

CMV; Epstein-Barr virus, EBR; rhinovirus; and, coronavirus.

4. The method of claim 1 wherein said pathogen is **HIV** and said molecule comprises a DNA sequence that encodes an **HIV** antigen.

5. The method of claim 1 wherein at least two non-identical DNA molecules are injected into skeletal muscle tissue of said individual at different sites on said individual's body, said bupivacaine being injected into each of the different sites of an individual; said non-identical DNA molecules each comprising DNA sequences encoding or more pathogen antigens of the same pathogen.

6. A method of immunizing an individual comprising: injecting in skeletal muscle tissue of said individual at a site on said individual's body, bupivacaine and a DNA molecule that comprises a DNA sequence encoding a hyperproliferative disease-associated protein operatively linked to regulatory sequences; wherein said DNA molecule is taken up by cells in said skeletal muscle tissue, said DNA sequence is expressed in said cells, and an immune response is generated against said hyperproliferative disease-associated protein.

7. The method of claim 6 wherein said DNA molecule comprises a DNA sequence encoding a target protein selected from the group consisting of: protein products of oncogenes myb, myc, fyn, ras, src, neu and protein products of translocation gene bcr/abl; P53; variable regions of **antibodies** made by B cell lymphomas; and variable regions of T cell receptors of T cell lymphomas.

8. A method of immunizing an individual comprising: injecting in skeletal muscle tissue of said individual, bupivacaine and a DNA molecule that comprises a DNA sequence that encodes an autoimmune disease-associated protein operatively linked to regulatory sequences wherein said DNA molecule is taken up by cells in said skeletal muscle tissue, said DNA sequence is expressed in said cells and an immune response is generated against said autoimmune disease-associated protein.

9. The method of claim 8 wherein said DNA molecule comprises a DNA sequence encoding a target protein selected from the group consisting of: variable regions of **antibodies** involved in B cell mediated autoimmune disease; and variable regions of T cell receptors involved in T cell mediated autoimmune disease.

L12 ANSWER 14 OF 21 USPTO on STN

96:113834 Bacterial expression vectors containing DNA encoding secretory signals of lipoproteins.

Stover, Charles K., Silver Spring, MD, United States

MedImmune, Inc., Gaithersburg, MD, United States (U.S. corporation)

US 5583038 19961210

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An expression vector for expressing a protein or polypeptide in bacterium, which comprises a first DNA sequence encoding at least a secretion signal of a lipoprotein, and a second DNA sequence encoding a protein or fragment thereof, or polypeptide or peptide heterologous to the bacterium which expresses the protein or fragment thereof, or polypeptide or peptide. The bacterium expresses a fusion protein comprising a lipoprotein or lipoprotein segment and the protein or fragment thereof, or polypeptide or peptide heterologous to the bacterium which expresses the protein or fragment thereof, or polypeptide or peptide. Such expression vectors increase the immunogenicity of the protein or fragment thereof, or polypeptide or peptide by enabling the protein or fragment thereof, or polypeptide or peptide to be expressed on the surface of the bacterium. Bacteria which may be transformed with the expression vector include mycobacteria such as BCG. The expression vectors of the present invention may be employed in the formulation of live bacterial vaccines against Lyme disease wherein the bacteria express a surface protein of *Borrelia burgdorferi*, the causative agent of Lyme disease.

CLM What is claimed is:

1. Recombinant mycobacteria transformed with DNA encoding a polypeptide comprising a lipoprotein secretion signal sequence and an antigen heterologous to the mycobacteria wherein the lipoprotein secretion signal causes the antigen to be produced as a lipoprotein.
2. The mycobacteria of claim 1 wherein the mycobacteria is BCG.
3. The mycobacteria of claim 2 wherein said DNA further includes a mycobacterial origin of replication.
4. The mycobacteria of claim 2 wherein said DNA further comprises a sequence encoding mycobacteriophage integration into a mycobacterial chromosome.
5. The mycobacteria of claim 1 wherein the lipoprotein secretion sequence is a secretion signal sequence of a mycobacterial lipoprotein.
6. The mycobacteria of claim 5 wherein said mycobacterial lipoprotein is an *M. tuberculosis* lipoprotein.
7. The mycobacteria of claim 6 wherein said *M. tuberculosis* lipoprotein is selected from the group consisting of the 19 kda and 38 kda antigens.
8. The mycobacteria of claim 6 wherein the mycobacteria is BCG.
9. The mycobacteria of claim 5 wherein the mycobacteria is BCG.
10. Mycobacteria transformed with DNA encoding a polypeptide, said

polypeptide comprising a lipoprotein secretion signal sequence a antigen which elicits **antibodies** against *Borrelia burgdorferi*, w the lipoprotein secretion signal causes the antigen to be produc lipoprotein.

11. The mycobacteria of claim 10 wherein said DNA encodes an ant derived from *Borrelia burgdorferi*.

12. The mycobacteria of claim 11 wherein said antigen is selecte the group consisting of Outer Surface Protein A antigen and an O Surface Protein B antigen.

13. The mycobacteria of claim 10 wherein said mycobacteria is BC

14. The mycobacteria of claim 13 wherein the antigen is an Outer Protein A antigen.

15. The mycobacteria of claim 14 wherein said lipoprotein secret signal sequence is the lipoprotein secretion signal sequence of Surface Protein A.

16. The mycobacteria of claim 10 wherein the lipoprotein secreti signal sequence is a secretion signal sequence of a mycobacteria lipoprotein.

17. The mycobacteria of claim 16 wherein said mycobacterial lipo is an *M. tuberculosis* lipoprotein.

18. The mycobacteria of claim 17 wherein said *M. tuberculosis* lipoprotein is selected from the group consisting of the 19 kda kda antigens.

19. The mycobacteria of claim 16 wherein the mycobacteria is BCG

20. The mycobacteria of claim 10 wherein the antigen is an Outer Protein A antigen.

21. A method of protecting an animal against Lyme disease, compr administering to an animal the mycobacteria of claim 10 in an am effective to protect an animal against Lyme disease.

22. The method of claim 21 wherein said DNA encodes an antigen d from *Borrelia burgdorferi*.

23. The method of claim 22 wherein said antigen is selected from group consisting of an Outer Surface Protein A antigen and Outer Protein B antigen.

24. The method of claim 22 wherein the lipoprotein secretion sig sequence is a secretion signal sequence of a mycobacterial lipop

25. The method of claim 24 wherein said mycobacterial lipoprotein is M. tuberculosis lipoprotein.
26. The method of claim 25 wherein said M. tuberculosis lipoprotein is selected from the group consisting of the 19 kda and 38 kda anti
27. The method of claim 22 wherein the antigen is an Outer Surface Protein A antigen.
28. The method of claim 27 wherein the mycobacteria is BCG.
29. The method of claim 21 wherein the mycobacteria is BCG.
30. The method of claim 29 wherein the antigen is an Outer Surface Protein A antigen.
31. The method of claim 30 wherein said lipoprotein secretion signal sequence is the lipoprotein secretion signal sequence of Outer Surface Protein A.

L12 ANSWER 15 OF 21 USPTO on STN

96:111154 Multiple antigen peptide system having adjuvant properties, v prepared therefrom and methods of use thereof.

Tam, James P., 607 S. Wilson Blvd., Nashville, TN, United States 3
US 5580563 19961203

WO 9322343 19931111

APPLICATION: US 1994-331489 19941228 (8)

<-

WO 1993-US4179 19930503 19941228 PCT 371 date 19941228 PCT 102(e)

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A multiple antigenic peptide system is disclosed that comprises dendritic core and peptide and a lipophilic anchoring moiety. This particular combination has as an advantage that it eliminates the need for the inclusion of adjuvants found to be toxic to humans, and facilitates the exponential amplification of the antigenic potential of a vaccine prepared therefrom, as noncovalent amplification by a micellar form is possible. Further, multiple different antigenic peptides may be attached so that the system may be prepared for administration to concurrently treat diverse ailments, such as for example, AIDS and influenza. The present multiple antigen peptide system is capable of eliciting an immune response when injected into a mammal and accordingly, vaccines prepared from the system and methods of use including therapeutic protocols are included.

CLM What is claimed is:

1. A multiple antigen peptide system comprising a dendritic core which are covalently attached at least one peptide and a lipophilic membrane anchoring moiety, wherein said multiple antigen peptide exhibits adjuvant properties and when injected into a mammal, is

of eliciting a full immune response provided by both humoral and mediated immunities including a cytotoxic T lymphocyte immune re

2. The multiple antigen peptide system of claim 1 wherein said lipophilic membrane anchoring moiety comprises a constituent sel from the group consisting of a lipoamino acid, a liposome, a sap derivative alone or in admixture with cholesterol, and a suitabl surfactant material.

3. The multiple antigen peptide system of claim 2, wherein said lipophilic membrane anchoring moiety comprises a lipoamino acid.

4. The multiple antigen peptide system of claim 1 wherein said d core comprises a bifunctional unit.

5. The multiple antigen peptide system of claim 1 further compri covalently attached T cell epitope.

6. The multiple antigen peptide system of claim 3 wherein said l acid is derived from amino acids selected from the group consist cysteine, lysine, serine and mixtures thereof.

7. The multiple antigen peptide system of claim 6 wherein said lipophilic membrane anchoring moiety comprises tripalmitoyl-S-glycerylcysteine.

8. The multiple antigen peptide system of claim 6 wherein said lipophilic membrane anchoring moiety comprises dipalmitoyl-S-glycerylcysteine.

9. The multiple antigen peptide system of claim 6 wherein said lipophilic membrane anchoring moiety comprises palmitoyl lysine.

10. The multiple antigen peptide system of claim 3 wherein said lipoamino acid is covalently attached through a peptide bond to acid polymer comprising a peptide.

11. The multiple antigen peptide system of claim 10 wherein said is a lipopeptide.

12. The multiple antigen peptide system of claim 5 wherein said epitope is covalently linked to said peptide.

13. The multiple antigen peptide system of claim 12 wherein said epitope is covalently linked in tandem to said peptide.

14. The multiple antigen peptide system of claim 5 wherein said epitope is at least seven amino acids long.

15. The multiple antigen peptide system of claim 5 wherein the T

epitope is a cytotoxic T cell epitope.

16. The multiple antigen peptide system of claim 5 wherein the T epitope is a helper T cell epitope.

17. The multiple antigen peptide system of claim 5 wherein the T epitope is derived from an **HIV-1** protein.

18. The multiple antigen peptide system of claim 17 wherein the protein is the **HIV-1** envelope glycoprotein.

19. The multiple antigen peptide system of claim 1 wherein said is encapsulated within a liposome.

20. The multiple antigen peptide system of claim 1 wherein said dendritic core comprises lysine.

21. The multiple antigen peptide system of claim 1 wherein said is between 10 and 40 amino acids long.

22. The multiple antigen peptide system of claim 5 further comprising B cell epitope.

23. The multiple antigen peptide system of claim 22 wherein the epitope and the T cell epitope are linked on the same functional of the dendritic core.

24. The multiple antigen peptide system of claim 4 wherein said dendritic core is tetravalent.

25. The multiple antigen peptide system of claim 2 wherein said surfactant material comprises a mixture of long chain polyoxyeth and polyoxypropylenes.

26. The multiple antigen peptide system of claim 4 wherein the bifunctional unit comprises an amino acid selected from the group consisting of cysteine, lysine, aspartic acid, glutamic acid, an ornithine.

27. The multiple antigen peptide system of claim 26 comprising eight free functional groups in the dendritic core and eight peptides, each of the eight peptides is attached to each of the eight free functional groups, thereby forming an octavalent multiple peptide antigen.

28. The multiple antigen peptide system of claim 27 further comprising eight covalently attached T cell epitopes.

29. The multiple antigen peptide system of claim 28 wherein the epitopes are derived from an **HIV-1** protein.

30. The multiple antigen peptide system of claim 28 wherein the lipophilic membrane anchoring moiety comprises a constituent selected from the group consisting of a lipoamino acid, a liposome, a sap derivative alone or in admixture with cholesterol, and a suitable surfactant material.

31. The multiple antigen peptide system of claim 30 wherein the lipophilic membrane anchoring moiety is a lipoamino acid derived amino acid selected from the group consisting of cysteine, lysine, serine and mixtures thereof.

32. The multiple antigen peptide system of claim 30 wherein the lipophilic membrane anchoring moiety is a lipoamino acid selected from the group consisting of tripalmitoyl-S-glycerylcysteine, dipalmitoyl-S-glycerylcysteine, and palmitoyl lysine.

33. A method for generating **antibodies** in a mammal, said method comprising administering to said mammal an **antibody**-generating system of the multiple antigen peptide system of claim 1.

34. A method for generating **antibodies** in a mammal said method comprising administering to said mammal an **antibody**-generating system of the multiple antigen peptide system of claim 32.

35. A method for generating **antibodies** in a mammal said method comprising administering to said mammal an **antibody**-generating system of the multiple antigen peptide system of claim 23.

36. A method for generating **antibodies** in a mammal said method comprising administering to said mammal an **antibody**-generating system of the multiple antigen peptide system of claim 5.

L12 ANSWER 16 OF 21 USPTAFULL on STN

95:71261 Non-infectious **HIV** particles lacking long terminal repeats.

Haynes, Joel, Middleton, WI, United States

Klein, Michel H., Willowdale, Canada

Rovinski, Benjamin, Thornhill, Canada

Cao, Shi X., Etobicoke, Canada

Connaught Laboratories Limited, Willowdale, Canada (non-U.S. corporate)
US 5439809 19950808

APPLICATION: US 1992-839751 19920615 (7)

<-

PRIORITY: GB 1989-23123 19891013

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An immunogenic **HIV** retrovirus-like particle which is non-infectious and non-replicating and which is useful as a candidate vaccine against **HIV** infection, is produced by genetic engineering. A DNA molecule comprising the **HIV** genome devoid of long terminal repeats

incorporated into an expression vector, which is introduced into mammalian cells for expression of the **HIV** retrovirus-like particle. What is claimed is:

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(iii) NUMBER OF SEQUENCES: 2

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 92 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

GATCTCG GACCGCCTACAATAAAAGAAAAGGATACATATAGGAAGCCTGGCGGATGTTA60
TTTTCTTTTTCCTATGTATATCCTGGTCCCTC92

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 88 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

CCAGGGAGAGCATTTTATACAACAAAAAATATAATAGGAACGCGTATCGTAAAATATGTT60
GTTTTTTATATTATCCTTGCGCATCTAG 88

1. A genetically-engineered, non-infectious, non-replicating immunogenic **HIV** retrovirus-like particle, produced by: incorporating into an expression vector a DNA molecule comprising the **HIV** genome devoid of long terminal repeats, introducing the expression vector into mammalian cells, and expressing said DNA molecule in said mammalian cells to produce said **HIV** retrovirus-like particle.

2. The particle of claim 1 which is deficient in primer binding

3. The particle of claim 1 which is deficient in Integrase and V proteins.

4. The particle of claim 1 wherein a V3 neutralizing epitope from heterologous **HIV** isolate is inserted into a Bgl II site of the envelope glycoprotein.

5. A method for obtaining a non-infectious, non-replicating, immunogenic **HIV** retrovirus-like particle by genetic engineering, which comprises incorporating into an expression vector a DNA molecule comprising the **HIV** genome devoid of long terminal repeats, introducing the expression vector into mammalian cells, and expressing said DNA molecule in said mammalian cells to produce said **HIV** retrovirus-like particle.

vector into mammalian cells, and expressing said DNA molecule in mammalian cells to produce **HIV** retrovirus-like particles.

6. The method of claim 5 wherein said expression vector is plasm pHIV-SV.

7. The method of claim 5 wherein said expression vector is plasm pHIV-CHO-SV.

8. The method of claim 5 wherein said expression vector is plasm pHIV-Ad.

9. The method of claim 5 wherein said expression vector is plasm PMT-**HIV**.

10. The method of claim 5 wherein said expression vector is plas pV3Bg.

11. The method of claim 6 wherein said **HIV** genome further is de in primer binding site.

12. The method of claim 11 wherein said **HIV** genome further is deficient in genomic elements coding for Intergrass and Vif.

13. The method of claim 5 wherein said DNA molecule incorporated the expression vector is provided by a DNA molecule containing t characteristic genetic elements present in the SacI to XhoI frag spanning nucleotides 678 to 8944 of the genome of **HIV-1** BRU iso

L12 ANSWER 17 OF 21 USPATFULL on STN

95:3945 Molecular clones of bovine immunodeficiency-like virus.

Gonda, Matthew A., Walkersville, MD, United States

The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United Sta (U.S. government)

US 5380830 19950110

APPLICATION: US 1992-980324 19921124 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Biologically active proviral molecular clones of bovine immunodeficiency-like virus and cell lines infected with the sam been prepared. Various utilities of the clones are described.

CLM What is claimed is:

1. Isolated and purified BIV proviral DNA with the nucleotide se as shown in FIGS. 6A-6D.

2. An isolated and purified, infectious, proviral molecular clon which is clone BIV106.

3. An isolated and purified, infectious, proviral molecular clone which is clone BIV127.

L12 ANSWER 18 OF 21 USPATFULL on STN

94:44555 Drosophila cell lines expressing genes encoding MHC class I and B2-microglobulin and capable of assembling empty complexes and of making said cell lines.

Peterson, Per A., LaJolla, CA, United States

Jackson, Michael, Del Mar, CA, United States

Langlade-Demoyen, Pierre, Del Mar, CA, United States

Scripps Research Institute, LaJolla, CA, United States (U.S. corporation)
US 5314813 19940524

APPLICATION: US 1992-841662 19920219 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a rational, elegant means of producing and using Class I molecules to specifically activate CD8 in vitro, and their therapeutic applications in the treatment of a variety of conditions, including cancer, tumors or neoplasias, as well as viral, retroviral, autoimmune, and autoimmune-type diseases. The present invention also relates to vectors, cell lines, recombinant molecules encoding human β 2 microglobulin or Class I MHC molecule in soluble and insoluble form, and methods of producing same.

CLM What is claimed is:

1. A stable cell line comprising: a human class I MHC gene, operably linked to an inducible promoter, capable of expressing a human class I MHC antigen on induction of said promoter; a human β -2-microglobulin gene, operably linked to a second inducible promoter capable of expressing a human β -2-microglobulin protein, on induction of said second promoter; wherein said cell is capable of assembling said MHC class I antigen and said β -2-microglobulin protein into empty complexes, and transporting and anchoring said complexes to the surface of the cell in sufficient numbers to activate a population of T-cell lymphocytes against a selected peptide when the peptide is bound to said complexes.

2. A cell line of claim 1, wherein said first and second promoters are metallothionein promoters.

3. A cell line of claim 1, wherein said human class I MHC gene and said human β -2-microglobulin gene are integrated in the genome of said cell line.

4. A cell line of claim 3, wherein said human class I MHC gene and said human β -2-microglobulin gene are operably linked to polyadenylation sequences.

5. A cell line of claim 4, wherein said human class I MHC antigen

B27 or A2.1.

6. A cell line of claim 5, wherein said peptide is derived from **human immunodeficiency virus** protein.

7. A method of producing a cell line of claim 1 comprising: esta a culture of *Drosophila* cells; transfecting said culture with an expressible human class I MHC gene operably linked to an inducible promoter; and transfecting said culture with an expressible human β 2-microglobulin gene operably linked to a second inducible promoter.

8. The method of claim 7 wherein said human class I MHC gene and human β -2-M gene are/is operably linked to a transcribable polyadenylation site.

9. The method of claim 7 wherein said human class I MHC gene and human β -2-M gene are/is inserted into a pRmHa-3 vector.

L12 ANSWER 19 OF 21 USPATFULL on STN

93:52501 Characterization of replication competent human immunodeficient 2 proviral clone **HIV-2**_{SBL/ISY}.

Franchini, Genoveffa, Washington, DC, United States

Wong-Staal, Flossie, San Diego, CA, United States

Gallo, Robert, Bethesda, MD, United States

United States of America, Washington, DC, United States (U.S. govern
US 5223423 19930629

APPLICATION: US 1989-331212 19890331 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A complete genomic clone of **HIV-2** designated **HIV-2**_{SBL/ISY} was cloned from DNA of the neoplastic human cell line HUT78 infected the **HIV-2**_{SBL6669} viral isolate. The clone was sequenced and the sequence compared with those of known **HIV-2** isolates. The invention is advantageous for it provides an animal model for the study of HIV infection in man.

CLM What is claimed is:

1. An isolated and purified replication competent **HIV-2** provirus designated **HIV-2**_{SBL/ISY}.

2. The clone of claim 1 wherein said clone has the restriction pattern as shown in FIG. 1.

3. An isolated and purified DNA segment having the nucleotide sequence or a nucleotide sequence encoding one or more of the amino acid sequences as shown in FIG. 5.

L12 ANSWER 20 OF 21 USPATFULL on STN

93:31326 Gene expressing VPT protein and vectors expressing this protei
Haseltine, William A., Cambridge, MA, United States
Cohen, Eric, Brighton, MA, United States
Dana Farber Cancer Institute, Boston, MA, United States (U.S. corpo
US 5204258 19930420

APPLICATION: US 1989-360847 19890602 (7)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Viral protein T from **Human Immunodeficiency Virus** Type 1 (**HIV-1**
is disclosed. The protein has a molecular weight of approximatel
and is produced by the vpt gene of **HIV-1**. This protein is antig
Vectors capable of expressing the vpt protein are also described

CLM What is claimed is:

1. A DNA segment containing a functional vpt gene but not the en
HIV genome, wherein the DNA segment will not express functional
protein having the ability to trans-activate.

2. A vector containing: (a) a nucleotide segment containing a su
number of nucleotides corresponding to a region extending from t
initiation codon and extending through the T open reading frame
HIV genome, to express viral protein T, wherein the T open readi
frame is in the same reading frame as the tat initiation codon w
the vector will not express functional tat protein having the ab
trans-activate, and wherein the vector does not contain the enti
genome; and (b) a protomer upstream of the nucleotide segment.

3. The vector of claim 2, wherein the nucleotide segment is DNA.

4. The vector of claim 2, wherein the nucleotide segment is RNA.

5. The vector of claim 3, wherein the promoter is a viral promot
the vector also contains an enhancer and polyadenylation sequenc

6. The vector of claim 2 wherein the **HIV** genome is **HIV-1**.

7. A cell line transformed by the vector of claim 2.

L12 ANSWER 21 OF 21 USPATFULL on STN

92:46989 Multilayer solid phase immunoassay support and method of use.

Chan, Emerson W., Libertyville, IL, United States
Schulze, Werner, Waukegan, IL, United States
Robey, William G., Libertyville, IL, United States
Braun, Brian P., Gurnee, IL, United States
Daluga, Cynthia K., Lindenhurst, IL, United States
Kapsalis, Andreas A., Evanston, IL, United States
Knigge, Kevin M., Gurnee, IL, United States
Stephens, John E., Chicago, IL, United States

Stojak, II, Joseph J., Waukegan, IL, United States
Vallaris, David S., Grayslake, IL, United States
Durley, deceased, Benton A., late of Antioch, IL, United States by
W. Durley; executrix
Defreese, James D., Lindenhurst, IL, United States
Merkh, Carl W., Lindenhurst, IL, United States
Abbott Laboratories, Abbott Park, IL, United States (U.S. corporati
US 5120662 19920609
APPLICATION: US 1990-532489 19900604 (7) <-
DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An immunoassay which is capable of simultaneously detecting any number of antigens of one infectious agent, or combinations of a of several infectious agents, or any desired number of immunoglo of one infectious agent, or combinations of immunoglobulins of s infectious agents on a single solid support. A test sample is co with a solid support on which one or more antigens are immobiliz discrete test sites. Antigen-**antibody** complexes are formed and detected on the solid support.

CLM What is claimed is:

1. An immunoassay to simultaneously detect the presence or amoun more than one **antibody** which may be present in a test sample, sa assay comprising: a. contacting a test sample of a species with solid support backed by inert plastic on which said porous solid more than one antigen is immobilized each on its own discrete te which is isolated by a surrounding moat created by a depression extends substantially through the porous solid support and which porous solid support was treated with a blocking reagent after s antigens were immobilized, for a time and under conditions suffi form antigen-**antibody** complexes; b. contacting said antigen-ant complexes with a conjugated signal generating system comprising anti-species **antibody** which anti-species **antibody** binds to the antigen-**antibody** complexes and which **antibody** is conjugated to detectable label which is capable of yielding a quantitatively measurable signal correlated to the signal of a normal negative sample to indicate **antibody** positive or **antibody** negative for t test sample; and c. detecting the presence of said antigen-anti complexes on said porous solid support by measuring the generate signal.

2. The immunoassay of claim 1 wherein the porous solid support i nitrocellulose.

3. The immunoassay of claim 1 wherein the discrete test site is immunodot blot.

4. The immunoassay of claim 1 wherein the **antibody** detected is selected from the group consisting of anti-HIV-1 **antibody**, anti-HIV-2 **antibody** and anti-HCV **antibody**.

5. The immunoassay of claim 1 wherein the **antibody** detected is anti-HIV-1 **antibody**.
6. The immunoassay of claim 1 wherein the **antibody** detected is anti-HIV-2 **antibody**.
7. The immunoassay of claim 1 wherein the **antibody** detected is anti-HCV **antibody**.
8. The immunoassay of claim 1 wherein the solid support is contacted with a blocking reagent prior to contacting the solid support with test sample.
9. The immunoassay of claim 1 wherein said label is selected from a group consisting of an enzyme, a luminescent label and a chemiluminescent label.
10. The immunoassay of claim 1 wherein said signal generating system is a biotin-anti-biotin amplifying system.
11. An immunoassay to simultaneously detect the presence or amount of more than one antigen which may be present in a test sample, said assay comprising:
a. contacting a test sample with a porous solid support on which said porous solid support more **antibody** is immobilized each on its own discrete test site which is isolated by a surrounding moat created by a depression which extends substantially through the porous solid support and which said porous solid support was treated with a blocking reagent after said antibodies were immobilized, for a time and under conditions sufficient to form antigen-**antibody** complexes;
b. contacting said antigen-**antibody** complexes with a conjugated signal generating system comprising one anti-antigen **antibody** which **antibody** binds to the antigen-**antibody** complexes and which **antibody** is conjugated to a detectable label which is capable of yielding a quantitatively measurable signal correlated to the signal of a normal negative sample to indicate antigen positive or antigen negative for the sample; and
c. detecting the presence of said antigen-**antibody** complexes on said porous solid support by measuring the generated signal.
12. The immunoassay of claim 11 wherein the porous solid support is nitrocellulose.
13. The immunoassay of claim 11 wherein the discrete test site is an immunodot blot.
14. The immunoassay of claim 11 wherein the antigen detected is from the group consisting of HIV-1, HIV-2 and HCV.
15. The immunoassay of claim 11 wherein the antigen detected is

16. The immunoassay of claim 11 wherein the antigen detected is
17. The immunoassay of claim 11 wherein the antigen detected is
18. The immunoassay of claim 11 wherein the solid support is con
with a blocking reagent prior to contacting the solid support wi
test sample.
19. The immunoassay of claim 11 wherein said label is selected f
group consisting of an enzyme, a luminescent label and a
chemiluminescent label.
20. The immunoassay of claim 11 wherein said signal generating s
a biotin-anti-biotin amplifying system.

=> d his

(FILE 'HOME' ENTERED AT 07:59:12 ON 04 APR 2005)

FILE 'USPATFULL' ENTERED AT 07:59:21 ON 04 APR 2005

```
L1          1 S US4808536/PN
L2          1 S US5001230/PN
L3          1 S US5874225/PN
            E WEINER DAVID B/IN
L4          57 S E1 OR E3
L5          33 S L4 AND (VPR OR VIRAL PROTEIN R)
L6          33 S L5 AND (ANTIBOD?)
L7          19 S L6 AND (ANTIBOD? (8W) VPR) OR (ANTIBOD? (8W) VIRAL PR
L8          18 S L7 AND (ANTIBOD?/CLM OR VPR/CLM OR VIRAL PROTEIN R/CL
L9          38258 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L10         728 S L9 AND (VPR OR VIRAL PROTEIN R)
L11         675 S L10 AND ANTIBOD?
L12         21 S L11 AND AY<1994
```

=> s l10 and (Vpr/clm or viral protein R/clm)

```
          156 VPR/CLM
          11272 VIRAL/CLM
          57583 PROTEIN/CLM
          298387 R/CLM
            4 VIRAL PROTEIN R/CLM
              ((VIRAL(W) PROTEIN(W) R)/CLM)
L13        141 L10 AND (VPR/CLM OR VIRAL PROTEIN R/CLM)
```

=> s l13 and antibod?/clm

```
          36027 ANTIBOD?/CLM
L14        40 L13 AND ANTIBOD?/CLM
```

=> s 114 and ay<1994
1977691 AY<1994
L15 2 L14 AND AY<1994

=> d 115,cbib,1-2

L15 ANSWER 1 OF 2 USPATFULL on STN

2005:471 **VPR** function and activity.

Weiner, David B., Merion, PA, United States

Levy, David Nathan, Philadelphia, PA, United States

Refaeli, Yosef, Philadelphia, PA, United States

The Trustees of the University of Pennsylvania, Philadelphia, PA, U
States (U.S. corporation)The Wistar Institute, Philadelphia, PA, Un
States (U.S. corporation)

US 6838236 B1 20050104

APPLICATION: US 1993-167608 19931215 (8)

<-

DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L15 ANSWER 2 OF 2 USPATFULL on STN

1999:24450 Identification of compounds that modulate **HIV-1 vpr** protein

Weiner, David B., Merion, PA, United States

Levy, David Nathan, Philadelphia, PA, United States

Trustees of The University of Pennsylvania, Philadelphia, PA, Unite
(U.S. corporation)The Wistar Institute, Philadelphia, PA, United St
(U.S. corporation)

US 5874225 19990223

APPLICATION: US 1993-19601 19930219 (8)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 07:59:12 ON 04 APR 2005)

FILE 'USPATFULL' ENTERED AT 07:59:21 ON 04 APR 2005

L1 1 S US4808536/PN

L2 1 S US5001230/PN

L3 1 S US5874225/PN

E WEINER DAVID B/IN

L4 57 S E1 OR E3

L5 33 S L4 AND (VPR OR VIRAL PROTEIN R)

L6 33 S L5 AND (ANTIBOD?)

L7 19 S L6 AND (ANTIBOD? (8W) VPR) OR (ANTIBOD? (8W) VIRAL PR

L8 18 S L7 AND (ANTIBOD?/CLM OR VPR/CLM OR VIRAL PROTEIN R/CL

L9 38258 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)

L10 728 S L9 AND (VPR OR VIRAL PROTEIN R)

L11 675 S L10 AND ANTIBOD?

L12 21 S L11 AND AY<1994
L13 141 S L10 AND (VPR/CLM OR VIRAL PROTEIN R/CLM)
L14 40 S L13 AND ANTIBOD?/CLM
L15 2 S L14 AND AY<1994

=> s l13 and ay<1994
1977691 AY<1994

L16 6 L13 AND AY<1994

=> s l16 not l15
L17 4 L16 NOT L15

=> d l17,cbib,1-4

L17 ANSWER 1 OF 4 USPATFULL on STN
2000:109568 Antisense viruses and antisense-ribozyme viruses.
Hu, Wen, Honolulu, HI, United States
Wang, Jie, Honolulu, HI, United States
Inpax, Inc., Honolulu, HI, United States (U.S. corporation)
US 6107062 20000822
APPLICATION: US 1992-921104 19920730 (7) <-
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 2 OF 4 USPATFULL on STN
1998:75745 DNA fragments obtained from a novel **human immunodeficiency virus** designated LAV_{MAL}.
Alizon, Marc, Paris, France
Sonigo, Pierre, Paris, France
Wain-Hobson, Simon, Montigny les Bretonneux, France
Montagnier, Luc, Le Plessis Robinson, France
Institut Pasteur, Paris, France (non-U.S. corporation)
US 5773602 19980630
APPLICATION: US 1993-154397 19931118 (8) <-
PRIORITY: FR 1986-401380 19860623
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 3 OF 4 USPATFULL on STN
97:106928 Nucleotide sequences derived from the genome of retroviruses
HIV-1, HIV-2 and SIV type, and their uses in particular for the
amplification of the genomes of these retroviruses and for the in v
diagnosis of the disease due to these viruses.
Moncany, Maurice, Paris, France
Montagnier, Luc, Le Plessis-Robinson, France
Institut Pasteur, France (non-U.S. corporation) Institut National de
Sante et de la Recherche Medicale, France (non-U.S. corporation)
US 5688637 19971118
APPLICATION: US 1993-160465 19931202 (8) <-
PRIORITY: FR 1989-7354 19890602

FR 1989-12371 19890920
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 4 OF 4 USPATFULL on STN

97:81129 Vectors containing **HIV** packaging sequences, packaging defectiv
HIV vectors, and uses thereof.

Sodroski, Joseph G., Medford, MA, United States

Haseltine, William A., Cambridge, MA, United States

Poznansky, Mark, Cambridge, MA, United States

Lever, Andrew, Pinner Middlesex, England

Gottlinger, Heinrich, Munich, Germany, Federal Republic of

Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corpo

US 5665577 19970909

APPLICATION: US 1993-152902 19931115 (8)

<-

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 117,cbib,ab,clm,2

L17 ANSWER 2 OF 4 USPATFULL on STN

1998:75745 DNA fragments obtained from a novel **human immunodeficiency**
virus designated LAV_{MAL}.

Alizon, Marc, Paris, France

Sonigo, Pierre, Paris, France

Wain-Hobson, Simon, Montigny les Bretonneux, France

Montagnier, Luc, Le Plessis Robinson, France

Institut Pasteur, Paris, France (non-U.S. corporation)

US 5773602 19980630

APPLICATION: US 1993-154397 19931118 (8)

<-

PRIORITY: FR 1986-401380 19860623

DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel **human immunodeficiency virus** type 1 (**HIV-1**) isolate,
designated lymphadenopathy-associated virus strain MAL, or LAV_{MA}
was molecularly cloned and characterized. Nucleotide sequence an
demonstrated that the viral genome of LAV_{MAL} is 9229 nucleotides
long. This retrovirus contains the canonical gag, pol, and env g
well as ancillary genes encoding Vif (or Q), **Vpr** (or R), Tat (o
and Nef (or F). This virus differs significantly, at both the nu
and amino acid sequence levels, from prototypical **HIV** isolates
HTLV-III, LAV_{BRU}, and ARV). DNA fragments corresponding to the
various gene products and regulatory regions are disclosed. Thes
fragments are useful, inter alia, as probes in diagnostic assays
the generation of recombinant proteins.

CLM What is claimed is:

1. A DNA fragment having a nucleotide sequence selected from the
consisting of: a sequence having nucleotides 1 to 96, which is t

terminal repeat R region of LAV_{MAL} ; a sequence having nucleotid 97 to 179, which is the 5' long terminal repeat U5 region of LAV ; a sequence having nucleotides 8676 to 9133, which is the 3' lo terminal repeat U3 region of LAV_{MAL} ; a sequence having nucleoti 9134 to 9229, which is the 3' long terminal repeat U3 region of LAV_{MAL} ; a sequence having nucleotides 5405 to 5620, which is th tat coding region of LAV_{MAL} ; a sequence having nucleotides 5134 5421, which is the **vpr** coding region of LAV_{MAL} ; a sequence having nucleotides 8380 to 9006, which is the nef coding region LAV_{MAL} ; a sequence having nucleotides 350 to 1864, which is the gag coding region of LAV_{MAL} ; a sequence having nucleotides 1663 4668, which is the pol coding region of LAV_{MAL} ; a sequence havi nucleotides 5799 to 8375, which is the env coding region of LAV ; a sequence having nucleotides 764 to 1501, which is the gag p2 region of LAV_{MAL} ; a sequence having nucleotides 1502 to 1864, which is the gag p13 coding region of LAV_{MAL} ; a sequence having nucleotides 5799 to 5885, which corresponds to amino acids 1-33 env coding region of LAV_{MAL} ; a sequence having nucleotides 5886 7337, which corresponds to amino acids 34 to 530 of the gp110 en region of LAV_{MAL} ; a sequence having nucleotides 5895 to 6176, which corresponds to amino acids 37 to 130 of the env coding reg LAV_{MAL} ; a sequence having nucleotides 6399 to 6635, which corresponds to amino acids 211 to 289 of the env coding region o LAV_{MAL} ; a sequence having nucleotides 7212 to 7337, which corresponds to amino acids 488 to 530 of the env coding region o LAV_{MAL} ; a sequence having nucleotides 7215 to 7604, which corresponds to amino acids 490 to 620 of the env coding region o LAV_{MAL} ; and a sequence having nucleotides 7782 to 7844, which corresponds to amino acids 680 to 700 of the env coding region o LAV_{MAL}.

2. The DNA fragment as claimed in claim 1, wherein said fragment operatively linked to a promoter sequence.

3. A DNA fragment as claimed in claim 1, wherein said fragment h nucleotide sequence having nucleotides 1 to 96, which is the lon terminal repeat R region of LAV_{MAL}.

4. A DNA fragment as claimed in claim 1, wherein said fragment h sequence having nucleotides 97 to 179, which is the 5' long term repeat U5 region of LAV_{MAL}.

5. A DNA fragment as claimed in claim 1, wherein said fragment h

sequence having nucleotides 8676 to 9133, which is the 3' long t repeat U3 region of LAV_{MAL}.

6. A DNA fragment as claimed in claim 1, wherein said fragment h sequence having nucleotides 9134 to 9229, which is the 3' long t repeat U3 region of LAV_{MAL}.

7. A DNA fragment as claimed in claim 1, wherein said fragment h sequence having nucleotides 5405 to 5620, which is the tat codin of LAV_{MAL}.

8. A DNA fragment as claimed in claim 1, wherein said fragment h sequence having nucleotides 5134 to 5421, which is the vpr codi region of LAV_{MAL}.

9. A DNA fragment as claimed in claim 1, wherein said fragment h sequence having nucleotides 8380 to 9006, which is the nef codin of LAV_{MAL}.

10. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 350 to 1864, which is the gag coding of LAV_{MAL}.

11. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 1663 to 4668, which is the pol codin of LAV_{MAL}.

12. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 5799 to 8375, which is the env codin of LAV_{MAL}.

13. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 764 to 1501, which is the gag p25 co region of LAV_{MAL}.

14. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 1502 to 1864, which is the gag p13 c region of LAV_{MAL}.

15. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 5799 to 5885, which corresponds to a acids 1-33 of the env coding region of LAV_{MAL}.

16. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 5886 to 7337, which corresponds to a acids 34 to 530 of the gp110 env coding region of LAV_{MAL}.

17. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 5895 to 6176, which corresponds to acids 37 to 130 of the env coding region of LAV_{MAL}.

18. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 6399 to 6635, which corresponds to acids 211 to 289 of the env coding region of LAV_{MAL}.

19. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 7212 to 7337, which corresponds to acids 488 to 530 of the env coding region of LAV_{MAL}.

20. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 7215 to 7604, which corresponds to acids 490 to 620 of the env coding region of LAV_{MAL}.

21. A DNA fragment as claimed in claim 1, wherein said fragment sequence having nucleotides 7782 to 7844, which corresponds to acids 680 to 700 of the env coding region of LAV_{MAL}.

22. A recombinant vector comprising a DNA fragment of any one of 1-21.

23. A transformed host comprising the recombinant vector of claim

=> d his

(FILE 'HOME' ENTERED AT 07:59:12 ON 04 APR 2005)

FILE 'USPATFULL' ENTERED AT 07:59:21 ON 04 APR 2005

L1	1 S US4808536/PN
L2	1 S US5001230/PN
L3	1 S US5874225/PN
	E WEINER DAVID B/IN
L4	57 S E1 OR E3
L5	33 S L4 AND (VPR OR VIRAL PROTEIN R)
L6	33 S L5 AND (ANTIBOD?)
L7	19 S L6 AND (ANTIBOD? (8W) VPR) OR (ANTIBOD? (8W) VIRAL PR
L8	18 S L7 AND (ANTIBOD?/CLM OR VPR/CLM OR VIRAL PROTEIN R/CL
L9	38258 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L10	728 S L9 AND (VPR OR VIRAL PROTEIN R)
L11	675 S L10 AND ANTIBOD?
L12	21 S L11 AND AY<1994
L13	141 S L10 AND (VPR/CLM OR VIRAL PROTEIN R/CLM)
L14	40 S L13 AND ANTIBOD?/CLM

L15 2 S L14 AND AY<1994
L16 6 S L13 AND AY<1994
L17 4 S L16 NOT L15

=> file wpids

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
172.84	173.05

FILE 'WPIDS' ENTERED AT 08:20:18 ON 04 APR 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE LAST UPDATED: 1 APR 2005 <20050401/UP>
MOST RECENT DERWENT UPDATE: 200521 <200521/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
<http://thomsonderwent.com/coverage/latestupdates/> <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
GUIDES, PLEASE VISIT:
<http://thomsonderwent.com/support/userguides/> <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: <http://www.thomsonderwent.com/dwpifv> <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
PLEASE CHECK:
<http://thomsonderwent.com/support/dwpiref/reftools/classification/code>
FOR DETAILS. <<<

=> e weiner david b/in

E1	8	WEINER D P/IN
E2	2	WEINER D S/IN
E3	0 -->	WEINER DAVID B/IN
E4	3	WEINER E/IN
E5	1	WEINER E J/IN
E6	1	WEINER E R/IN
E7	1	WEINER E S/IN
E8	2	WEINER E T/IN
E9	7	WEINER F/IN
E10	1	WEINER F M/IN
E11	9	WEINER G/IN
E12	2	WEINER G A/IN

=> e weiner d b/in

E1	18	WEINER D/IN
E2	2	WEINER D A/IN
E3	66 -->	WEINER D B/IN
E4	1	WEINER D D/IN
E5	2	WEINER D L/IN
E6	2	WEINER D M/IN
E7	8	WEINER D P/IN
E8	2	WEINER D S/IN
E9	3	WEINER E/IN
E10	1	WEINER E J/IN
E11	1	WEINER E R/IN
E12	1	WEINER E S/IN

=> s e3

L18 66 "WEINER D B"/IN

=> s l18 and (Vpr or viral protein R)

189 VPR
25368 VIRAL
125679 PROTEIN
516594 R
10 VIRAL PROTEIN R
(VIRAL(W) PROTEIN(W) R)

L19 10 L18 AND (VPR OR VIRAL PROTEIN R)

=> d l19,bib,1-10

L19 ANSWER 1 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 2003-449457 [42] WPIDS

DNN N2003-358565 DNC C2003-119425

TI Identifying compounds that inhibit HIV **Vpr** binding to apoptosis i
factor (AIF), useful for treating cancer, inflammatory disease or
autoimmune disease, comprises contacting HIV **Vpr** and AIF in the p
of a test compound.

DC B04 D16 S03

IN MUTHUMANI, K; **WEINER, D B**

PA (UYPE-N) UNIV PENNSYLVANIA; (MUTH-I) MUTHUMANI K; (WEIN-I) WEINER
CYC 101

PI WO 2003040415 A1 20030515 (200342)* EN 11

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC
NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU
ZW

EP 1397520 A1 20040317 (200420) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK
 RO SE SI TR
 AU 2002310158 A1 20030519 (200464)
 US 2005026138 A1 20050203 (200511)
 ADT WO 2003040415 A1 WO 2002-US16731 20020528; EP 1397520 A1 EP 2002-
 20020528, WO 2002-US16731 20020528; AU 2002310158 A1 AU 2002-3101
 20020528; US 2005026138 A1 Provisional US 2001-293570P 20010525,
 2002-US16731 20020528, US 2004-478742 20040802
 FDT EP 1397520 A1 Based on WO 2003040415; AU 2002310158 A1 Based on WO
 2003040415
 PRAI US 2001-293570P 20010525; US 2004-478742 20040802

L19 ANSWER 2 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text

AN 2003-381674 [36] WPIDS

DNC C2003-101425

TI Treatment of sepsis and systemic inflammatory response syndrome in
 administration of a composition comprising **viral protein R** of HIV
 its fragment or nucleic acid encoding the protein or its fragment.

DC B04 B05 D16

IN KARUPPIAH, M; **WEINER, D B**; MUTHAMANI, K; MUTHUMANI, K

PA (UYPE-N) UNIV PENNSYLVANIA; (MUTH-I) MUTHUMANI K; (WEIN-I) WEINER

CYC 101

PI WO 2003030827 A2 20030417 (200336)* EN 18

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE
 MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH
 RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU
 ZW

EP 1453548 A2 20040908 (200459) EN

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU
 MK NL PT RO SE SI SK TR

AU 2002362753 A1 20030422 (200461)

US 2005042202 A1 20050224 (200515)

ADT WO 2003030827 A2 WO 2002-US32084 20021007; EP 1453548 A2 EP 2002-
 20021007, WO 2002-US32084 20021007; AU 2002362753 A1 AU 2002-3627
 20021007; US 2005042202 A1 Provisional US 2001-327270P 20011005,
 2002-US32084 20021007, US 2004-491800 20041007

FDT EP 1453548 A2 Based on WO 2003030827; AU 2002362753 A1 Based on WO
 2003030827

PRAI US 2001-327270P 20011005; US 2004-491800 20041007

L19 ANSWER 3 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text

AN 2003-167364 [16] WPIDS

DNN N2003-132260 DNC C2003-043493

TI Non-cellular particle (e.g. of human immunodeficiency virus), for
 delivery, prophylaxis against viruses and cancer, and treating aut

diseases, comprises a nucleic acid and/or a fusion protein having ligand.

DC B04 C06 D16 P33

IN MUTHAMANI, K; RAMANATHAN, M P; **WEINER, D B**; ZHANG, D; MUTHUMANI, RAMANTHAN, M P

PA (UYPE-N) UNIV PENNSYLVANIA; (MUTH-I) MUTHUMANI K; (RAMA-I) RAMANT (WEIN-I) WEINER D B; (ZHAN-I) ZHANG D

CYC 100

PI WO 2002100317 A2 20021219 (200316)* EN 31
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC NL OA PT SD SE SL SZ TR TZ UG ZM ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZW

AU 2002329176 A1 20021223 (200452)
 US 2005054104 A1 20050310 (200519)

ADT WO 2002100317 A2 WO 2002-US16681 20020528; AU 2002329176 A1 AU 20020528; US 2005054104 A1 Provisional US 2001-293683P 20010525, 2002-US16681 20020528, US 2004-478896 20040830

FDT AU 2002329176 A1 Based on WO 2002100317

PRAI US 2001-293683P 20010525; US 2004-478896 20040830

L19 ANSWER 4 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN Full Text

AN 2001-662940 [76] WPIDS

DNC C2001-194732

TI Delivering polypeptide for gene therapy comprises administering ve comprising a nucleic acid encoding **viral protein R** (from HIV), it fragment or nucleic acid encoding the protein.

DC B04 D16

IN AYYAVOO, V; MUTHUMANI, K; **WEINER, D B**

PA (UYPE-N) UNIV PENNSYLVANIA; (MUTH-I) MUTHUMANI K; (WEIN-I) WEINER

CYC 96

PI WO 2001074163 A1 20011011 (200176)* EN 61
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001049576 A 20011015 (200209)
 US 2004028651 A1 20040212 (200412)
 EP 1404705 A1 20040407 (200425) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK RO SE SI TR

ADT WO 2001074163 A1 WO 2001-US10028 20010329; AU 2001049576 A AU 200120010329; US 2004028651 A1 WO 2001-US10028 20010329, US 2002-3112 20021213; EP 1404705 A1 EP 2001-922815 20010329, WO 2001-US10028

FDT AU 2001049576 A Based on WO 2001074163; EP 1404705 A1 Based on WO 2001074163

PRAI US 2000-231141P 20000908; US 2000-193495P 20000331;
US 2002-311260 20021213

L19 ANSWER 5 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 1999-277596 [23] WPIDS

CR 1999-181154 [15]

DNC C1999-081631

TI Human **Vpr** interacting protein for, e.g. treatment of cancer.

DC B04 D16

IN AYYAVOO, V; MAHALINGAM, S; PATEL, M; **WEINER, D B**

PA (UYPE-N) UNIV PENNSYLVANIA; (AYYA-I) AYYAVOO V; (MAHA-I) MAHALING
(PATE-I) PATEL M; (WEIN-I) WEINER D B

CYC 83

PI WO 9919359 A1 19990422 (199923)* EN 58
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI
GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
US UZ VN YU ZW

AU 9897980 A 19990503 (199937)

EP 1021464 A1 20000726 (200037) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU NL PT SE

KR 2001040257 A 20010515 (200167)

JP 2001522582 W 20011120 (200204) 78

AU 745235 B 20020314 (200231)

US 6448078 B1 20020910 (200263)

US 2003143735 A1 20030731 (200354)

ADT WO 9919359 A1 WO 1998-US21432 19981009; AU 9897980 A AU 1998-9798
19981009; EP 1021464 A1 EP 1998-952230 19981009, WO 1998-US21432
KR 2001040257 A KR 2000-703859 20000410; JP 2001522582 W WO 1998-
19981009, JP 2000-515930 19981009; AU 745235 B AU 1998-97980 1998
6448078 B1 WO 1998-US21432 19981009, US 2000-529245 20001017; US
2003143735 A1 Cont of WO 1998-US21432 19981009, Cont of US 2000-5
20001017, US 2003-208338 20030227

FDT AU 9897980 A Based on WO 9919359; EP 1021464 A1 Based on WO 991935
2001522582 W Based on WO 9919359; AU 745235 B Previous Publ. AU 98
Based on WO 9919359; US 6448078 B1 Based on WO 9919359; US 2003143
Cont of US 6448078

PRAI US 1997-949202 19971010; US 2000-529245 20001017;
US 2003-208338 20030227

L19 ANSWER 6 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 1999-181154 [15] WPIDS

CR 1999-277596 [23]

DNN N1999-132965 DNC C1999-052973

TI Conjugate composition comprising HIV-1 **Vpr** protein fragment - us
 inhibit cell proliferation, and treating hyperproliferative diseases
 DC B04 D16 S03
 IN AYYAVOO, V; KIEBER-EMMONS, T; MAHALINGAM, S; PATEL, M; **WEINER, D**
 MAHALINGHAM, S; WILLIAMS, W V
 PA (UYPE-N) UNIV PENNSYLVANIA
 CYC 83
 PI WO 9909412 A1 19990225 (199915)* EN 64
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC
 OA PT SD SE SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI
 GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
 MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
 US UZ VN YU ZW
 AU 9887838 A 19990308 (199929)
 US 6060587 A 20000509 (200030)
 EP 1012603 A1 20000628 (200035) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
 US 6087486 A 20000711 (200037)#
 US 6172201 B1 20010109 (200104)
 AU 753031 B 20021003 (200301)
 EP 1012603 B1 20041027 (200471) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
 US 6818627 B1 20041116 (200475)
 DE 69827284 E 20041202 (200479)
 ADT WO 9909412 A1 WO 1998-US16890 19980814; AU 9887838 A AU 1998-8783
 19980814; US 6060587 A CIP of US 1996-593695 19960129, Provisional
 1997-55754P 19970814, US 1997-949202 19971010; EP 1012603 A1 EP
 1998-939404 19980814, WO 1998-US16890 19980814; US 6087486 A Cont
 1996-593695 19960129, US 1998-14877 19980128; US 6172201 B1 CIP of
 1996-593695 19960129, Provisional US 1997-55754P 19970814, Cont o
 1997-949202 19971010, US 1999-418175 19991013; AU 753031 B AU 1998
 19980814; EP 1012603 B1 EP 1998-939404 19980814, WO 1998-US16890
 US 6818627 B1 Provisional US 1997-55754P 19970814, WO 1998-US1689
 19980814, US 2000-485421 20001005; DE 69827284 E DE 1998-627284 1
 EP 1998-939404 19980814, WO 1998-US16890 19980814
 FDT AU 9887838 A Based on WO 9909412; EP 1012603 A1 Based on WO 990941
 753031 B Previous Publ. AU 9887838, Based on WO 9909412; EP 101260
 Based on WO 9909412; US 6818627 B1 Based on WO 9909412; DE 6982728
 Based on EP 1012603, Based on WO 9909412
 PRAI US 1997-55754P 19970814; US 1996-593695 19960129;
 US 1997-949202 19971010; US 1998-14877 19980128;
 US 1999-418175 19991013; US 2000-485421 20001005

 L19 ANSWER 7 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text
 AN 1996-188141 [19] WPIDS
 DNC C1996-060041
 TI Inhibition of cell proliferating and lymphocyte activation - by c
 cells with HIV **vpr** protein or **vpr**-encoding nucleic acid.

DC B04 D16
 IN AYYAROO, V; LEVY, D N; REFAELI, Y; **WEINER, D B**; WILLIAMS, W V; AY
 PA (APOL-N) APOLLON INC; (UYPE-N) UNIV PENNSYLVANIA; (LEVY-I) LEVY D
 (REFA-I) REFAELI Y; (WEIN-I) WEINER D B
 CYC 64
 PI WO 9608970 A1 19960328 (199619)* EN 66
 RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE
 W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS
 KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU
 SG SI SK TJ TM TT UA UG US UZ VN
 AU 9537276 A 19960409 (199629)
 US 5763190 A 19980609 (199830)
 US 6667157 B1 20031223 (200408)
 US 2004259827 A1 20041223 (200504)
 ADT WO 9608970 A1 WO 1995-US12344 19950921; AU 9537276 A AU 1995-3727
 19950921; US 5763190 A US 1994-309644 19940921; US 6667157 B1 CIP
 1994-309644 19940921, WO 1995-US12344 19950921, US 1997-809186 19
 US 2004259827 A1 Cont of WO 1995-US12344 19950921, Cont of US 1997
 19970624, US 2003-734024 20031211
 FDT AU 9537276 A Based on WO 9608970; US 6667157 B1 CIP of US 5763190,
 on WO 9608970; US 2004259827 A1 Cont of US 6667157
 PRAI US 1994-309644 19940921; US 1997-809186 19970624;
 US 2003-734024 20031211

L19 ANSWER 8 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text

AN 1996-020283 [02] WPIDS
 DNN N1996-016947 DNC C1996-006945
 TI Method of treating H.I.V. infection - involves using compounds whi
 prevent H.I.V. replication by blocking interaction of vapour with
 target rip-1.

DC B04 D16 S03
 IN REFAELI, Y; **WEINER, D B**; LEVY, D M; LEVY, D N
 PA (UYPE-N) UNIV PENNSYLVANIA
 CYC 65

PI WO 9531901 A1 19951130 (199602)* EN 65
 RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE
 W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS
 KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU
 SG SI SK TJ TM TT UA UG US UZ VN
 AU 9525880 A 19951218 (199611)
 EP 759693 A1 19970305 (199714) EN
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
 US 5639598 A 19970617 (199730) 15
 AU 690694 B 19980430 (199829)
 US 5780220 A 19980714 (199835)
 EP 759693 B1 20031126 (200402) EN
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
 DE 69532197 E 20040108 (200411)
 ES 2210291 T3 20040701 (200444)

ADT WO 9531901 A1 WO 1995-US5981 19950517; AU 9525880 A AU 1995-25880 19950511; EP 759693 A1 EP 1995-920426 19950517, WO 1995-US5981 19 US 5639598 A US 1994-246177 19940519; AU 690694 B AU 1995-25880 1 US 5780220 A CIP of US 1994-246177 19940519, US 1995-382873 19950 759693 B1 EP 1995-920426 19950517, WO 1995-US5981 19950517; DE 69 DE 1995-632197 19950517, EP 1995-920426 19950517, WO 1995-US5981 ES 2210291 T3 EP 1995-920426 19950517

FDT AU 9525880 A Based on WO 9531901; EP 759693 A1 Based on WO 9531901 690694 B Previous Publ. AU 9525880, Based on WO 9531901; US 578022 of US 5639598; EP 759693 B1 Based on WO 9531901; DE 69532197 E Bas 759693, Based on WO 9531901; ES 2210291 T3 Based on EP 759693

PRAI US 1995-382873 19950203; US 1994-246177 19940519

L19 ANSWER 9 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN Full Text

AN 1995-231517 [30] WPIDS

DNC C1995-106867

TI Pure **vpr** receptor protein - useful to treat individuals exposed to and to identify anti-HIV agents that inhibit binding of **vpr** to th receptor.

DC B04

IN LEVY, D N; REFAELI, Y; WEINER, D B

PA (UYPE-N) UNIV PENNSYLVANIA

CYC 20

PI WO 9516705 A1 19950622 (199530)* EN 31

RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

W: AU CA JP US

AU 9513733 A 19950703 (199542)

US 5780238 A 19980714 (199835)

ADT WO 9516705 A1 WO 1994-US14532 19941215; AU 9513733 A AU 1995-1373 19941215; US 5780238 A CIP of US 1993-167519 19931215, WO 1994-US 19941215, US 1996-652572 19961024

FDT AU 9513733 A Based on WO 9516705; US 5780238 A Based on WO 9516705

PRAI US 1993-167519 19931215; US 1996-652572 19961024

L19 ANSWER 10 OF 10 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN Full Text

AN 1994-294323 [36] WPIDS

DNC C1994-134441

TI Use of **viral protein R** and nucleic acid - for inducing differentiation of cells and in screening assays, diagnosis and th e.g. HIV infection.

DC B04 D16

IN LEVY, D N; REFAELI, Y; WEINER, D B

PA (WEIN-I) WEINER D B; (LEVY-I) LEVY D N; (REFA-I) REFAELI Y; (LEVY M; (UYPE-N) UNIV PENNSYLVANIA; (WIST-N) WISTAR INST

CYC 51

PI WO 9419456 A1 19940901 (199436)* EN 114

RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE

W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB HU JP KP KR KZ

LV MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US UZ VN
 AU 9462524 A 19940914 (199502)
 ZA 9401111 A 19941130 (199503) 32
 EP 689586 A1 19960103 (199606) EN
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
 EP 689586 A4 19971229 (199840)
 US 5874225 A 19990223 (199915)
 IL 108707 A 19990620 (199937)
 US 2003207252 A1 20031106 (200374)
 MX 9401321 A1 20031001 (200466)
 US 6838236 B1 20050104 (200503)
 ADT WO 9419456 A1 WO 1994-US2191 19940222; AU 9462524 A AU 1994-62524
 19940222; ZA 9401111 A ZA 1994-1111 19940218; EP 689586 A1 EP 1994
 19940222, WO 1994-US2191 19940222; EP 689586 A4 EP 1994-909839 19
 US 5874225 A US 1993-19601 19930219; IL 108707 A IL 1994-108707 1
 US 2003207252 A1 CIP of US 1993-19601 19930219, Div ex US 1993-16
 19931215, US 2001-935100 20010822; MX 9401321 A1 MX 1994-1321 199
 6838236 B1 CIP of US 1993-19601 19930219, US 1993-167608 19931215
 FDT AU 9462524 A Based on WO 9419456; EP 689586 A1 Based on WO 9419456
 2003207252 A1 CIP of US 5874225; US 6838236 B1 CIP of US 5874225
 PRAI US 1993-167608 19931215; US 1993-19601 19930219;
 US 2001-935100 20010822

=> d his

(FILE 'HOME' ENTERED AT 07:59:12 ON 04 APR 2005)

FILE 'USPATFULL' ENTERED AT 07:59:21 ON 04 APR 2005

L1 1 S US4808536/PN
 L2 1 S US5001230/PN
 L3 1 S US5874225/PN
 E WEINER DAVID B/IN
 L4 57 S E1 OR E3
 L5 33 S L4 AND (VPR OR VIRAL PROTEIN R)
 L6 33 S L5 AND (ANTIBOD?)
 L7 19 S L6 AND (ANTIBOD? (8W) VPR) OR (ANTIBOD? (8W) VIRAL PR
 L8 18 S L7 AND (ANTIBOD?/CLM OR VPR/CLM OR VIRAL PROTEIN R/CL
 L9 38258 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
 L10 728 S L9 AND (VPR OR VIRAL PROTEIN R)
 L11 675 S L10 AND ANTIBOD?
 L12 21 S L11 AND AY<1994
 L13 141 S L10 AND (VPR/CLM OR VIRAL PROTEIN R/CLM)
 L14 40 S L13 AND ANTIBOD?/CLM
 L15 2 S L14 AND AY<1994
 L16 6 S L13 AND AY<1994
 L17 4 S L16 NOT L15

FILE 'WPIDS' ENTERED AT 08:20:18 ON 04 APR 2005

E WEINER DAVID B/IN


```

                E WEINER D B/IN
L18             66 S E3
L19             10 S L18 AND (VPR OR VIRAL PROTEIN R)

=> s (Vpr or viral protein R)
            189 VPR
            25368 VIRAL
            125679 PROTEIN
            516594 R
            10 VIRAL PROTEIN R
              (VIRAL(W) PROTEIN(W) R)
L20           189 (VPR OR VIRAL PROTEIN R)

=> s l20 and (Vpr/ab or viral protein R/ab)
'AB' IS NOT A VALID FIELD CODE
            0 VPR/AB
            0 VIRAL PROTEIN R/AB
L21           0 L20 AND (VPR/AB OR VIRAL PROTEIN R/AB)

=> s l20 and ay<1994
            4520355 AY<1994
              (AY<1994)
L22           32 L20 AND AY<1994

=> s l22 not l19
L23           30 L22 NOT L19

=> d l23,bib,1-30

L23 ANSWER 1 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2004-236717 [22] WPIDS
CR 1985-100790 [17]; 1986-119166 [18]; 1986-212111 [32]; 1986-313518
   1995-161085 [21]; 2002-711525 [77]; 2003-615327 [58]
DNC C2004-092505
TI New purified peptide encoded by the vpr gene of HIV-1, useful for
   preparing a composition for diagnosing or treating HIV infection.
DC B04 D16 S03
IN ALIZON, M; BARRE-SINOUSSE, F; CHAMARET, S; CHERMANN, J; CLAVEL, F;
   O; KRUST, B; MONTAGNIER, L; SONIGO, P; STEWART, C; WAIN-HOBSON, S
PA (CNRS) CENT NAT RECH SCI; (INSP) INST PASTEUR
CYC 12
PI US 6706268 B1 20040316 (200422)* 37
   EP 1231271 B1 20041229 (200502) EN
   R: AT BE CH DE FR GB IT LI LU NL SE
   DE 3588251 G 20050203 (200510)
ADT US 6706268 B1 Div ex US 1985-771248 19850830, Div ex US 1988-1586
   19880222, Div ex US 1992-953060 19921105, Div ex US 1994-195024
   19940214, Div ex US 1997-344449 19971231, US 2000-709316 20001113
   1231271 B1 Div ex EP 1991-113062 19851018, Related to EP 2001-111

```

19851018, EP 2002-8713 19851018; DE 3588251 G DE 1985-3588251
19851018, EP 2002-8713 19851018
FDT US 6706268 B1 Div ex US 5705612, Div ex US 6261564; EP 1231271 B1
EP 462627; DE 3588251 G Based on EP 1231271
PRAI GB 1984-29099 19841116; FR 1984-16013 19841018;
GB 1985-1473 19850121

L23 ANSWER 2 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2001-060089 [07] WPIDS
CR 2000-037081 [03]; 2000-125951 [11]
DNC C2001-016580
TI New altered major histocompatibility complex (MHC) class I determi
useful for eliciting an immune response and/or for immunizing agai
treating diseases, for example, multiple sclerosis, AIDS, toxic sh
snake bite.
DC B04 D16
IN ABASTADO, J; CASROUGE, A; KOURILSKY, P; LONE, Y; MOTTEZ, E; OJCIUS
PA (INRM) INST NAT SANTE & RECH MEDICAL; (INSP) INST PASTEUR
CYC 1
PI US 6153408 A 20001128 (200107)* 105
ADT US 6153408 A Cont of US 1991-792473 19911115, CIP of US 1991-8018
19911205, CIP of US 1993-72787 19930607, Cont of US 1993-117575
19930907, US 1995-370476 19950109
PRAI US 1993-117575 19930907; US 1991-792473 19911115;
US 1991-801818 19911205; US 1993-72787 19930607;
US 1995-370476 19950109

L23 ANSWER 3 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2000-037081 [03] WPIDS
CR 2000-125951 [11]; 2001-060089 [02]
DNC C2000-009448
TI Composition containing an antigen and altered major histocompatibi
Class II determinant, used to immunize against autoimmune diseases
acquired immune deficiency syndrome.
DC B04 D16
IN ABASTADO, J; KOURILSKY, P; MOTTEZ, E
PA (INRM) INSERM INST NAT SANTE & RECH MEDICALE; (INSP) INST PASTEUR
CYC 1
PI US 5976551 A 19991102 (200003)* 96
ADT US 5976551 A Cont of US 1991-792473 19911115, Div ex US 1991-8018
19911205, US 1995-484905 19950607
PRAI US 1991-792473 19911115; US 1991-801818 19911205;
US 1995-484905 19950607

L23 ANSWER 4 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1998-210039 [19] WPIDS
DNN N1998-166792 DNC C1998-066175

TI Colour image recording method using electrostatic latent image -
maintaining ratio of moving speed of two component roller and that
latent image carrier within predetermined range.

DC G08 P84

PA (XERF) FUJI XEROX KK

CYC 1

PI JP 2736970 B2 19980408 (199819)* 7
JP 63254472 A 19881021 (199819)

ADT JP 2736970 B2 **JP 1987-88627 19870413**; JP 63254472 A **JP 1987-88627**

FDT JP 2736970 B2 Previous Publ. JP 63254472

PRAI JP 1987-88627 19870413

L23 ANSWER 5 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 1997-538622 [50] WPIDS

CR 1990-378039 [51]

DNN N1997-448251 DNC C1997-172371

TI Oligo-nucleotide primers for amplifying retroviral nucleic acids
comprising conserved sequences of human immunodeficiency virus and
immunodeficiency virus genes.

DC B04 D16 S03

IN MONCANY, M; MONTAGNIER, L; LUC, M; MAURICE, M

PA (INRM) INSERM INST NAT SANTE & RECH MEDICALE; (INSP) INST PASTEUR;
INSERM INST NAT SANTE RE; (INRM) INST NAT SANTE & RECH MEDICALE

CYC 17

PI EP 806484 A2 19971112 (199750)* FR 23
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE

SG 47868 A1 19980417 (199827)

US 5786177 A 19980728 (199837)

EP 403333 B1 19991006 (199946) FR
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE

DE 69033311 E 19991111 (199954)

ES 2139567 T3 20000216 (200016)

JP 2000093187 A 20000404 (200027) 14

US 6194142 B1 20010227 (200114)

JP 3428012 B2 20030722 (200350) 23

US 2005037340 A1 20050217 (200514)

ADT EP 806484 A2 Div ex EP 1990-401520 19900605, EP 1997-110543 1990
SG 47868 A1 SG 1996-4845 19900605; US 5786177 A Cont of US 1992-8
19920121, Div ex US 1993-160465 19931202, US 1997-895231 19970716
403333 B1 EP 1990-401520 19900605, Related to EP 1997-110543 1990
DE 69033311 E DE 1990-633311 19900605, EP 1990-401520 19900605; E
2139567 T3 EP 1990-401520 19900605; JP 2000093187 A Div ex JP
1990-508911 19900605, JP 1999-270165 19900605; US 6194142 B1 Cont
US 1992-820599 19920121, Div ex US 1993-160465 19931202, Div ex U
1997-895231 19970716, US 1998-92077 19980605; JP 3428012 B2 JP
1990-508911 19900605, WO 1990-FR393 19900605; US 2005037340 A1 Co
US 1992-820599 19920121, Div ex US 1993-160465 19931202, Div ex U
1995-472928 19950607, US 2004-862363 20040608

FDT EP 806484 A2 Div ex EP 403333; US 5786177 A Div ex US 5688637; EP

B1 Related to EP 806484; DE 69033311 E Based on EP 403333; ES 2139
Based on EP 403333; US 6194142 B1 Div ex US 5688637, Div ex US 578
3428012 B2 Previous Publ. JP 04507043, Based on WO 9015066; US 200
A1 Div ex US 5688637
PRAI FR 1989-12371 19890920; FR 1989-7354 19890602;
WO 1990-FR393 19900506

L23 ANSWER 6 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1997-148339 [14] WPIDS
DNN N1997-122593 DNC C1997-047315
TI Image formation for negatively charged toner for electrophotograph
devices - by using specified large contact angle of water in one-
system contg. coating matter with lubricated surface in holder, fo
multicoloured development.
DC G08 P84
PA (CANO) CANON INC
CYC 1
PI JP 2584281 B2 19970226 (199714)* 8
JP 02010387 A 19900116 (199714)
ADT JP 2584281 B2 **JP 1988-159349 19880629**; JP 02010387 A **JP 1988-1593
19880629**
FDT JP 2584281 B2 Previous Publ. JP 02010387
PRAI JP 1988-159349 19880629

L23 ANSWER 7 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1994-279391 [34] WPIDS
DNC C1994-127476
TI Multiple gene mutants of human immunodeficiency virus - provide s
attenuated vaccine for treatment and prophylaxis of HIV.
DC B04 D16
IN LOONEY, D J; WONG-STAAAL, F; WONGSTAAL, F
PA (REGC) UNIV CALIFORNIA
CYC 45
PI WO 9417825 A1 19940818 (199434)* EN 28
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AU BB BG BR BY CA CZ FI HU JP KP KR KZ LK LV MG MN MW NO NZ
RU SD SK UA UZ VN
AU 9458487 A 19940829 (199501)
ADT WO 9417825 A1 **WO 1993-US12088 19931213**; AU 9458487 A **WO 1993-US12
19931213, AU 1994-58487 19931213**
FDT AU 9458487 A Based on WO 9417825
PRAI US 1993-14318 19930205

L23 ANSWER 8 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1994-024712 [03] WPIDS
DNN N1994-019213 DNC C1994-011493
TI Fabricator of rapidly cooled metal sheets etc. - consists of part

crucible with porous refractory yielding non deformable brazing al
DC M22 P53
IN CHEBOTARENKO, V YA; KULESHOV, B M; OVCHAROV, V P
PA (CHRN) FERROUS METALLURGY INST
CYC 1
PI SU 1785786 A1 19930107 (199403)* 5
ADT SU 1785786 A1 **SU 1989-4737120 19890913**
PRAI SU 1989-4737120 19890913

L23 ANSWER 9 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1993-405823 [50] WPIDS
DNN N1993-314044 DNC C1993-180402
TI Hybrid SIV-HIV-1 viral vectors - used to provide animal models for
infection or a therapeutic agents or in vaccines for HIV-1.
DC B04 D16 P14
IN HASELTINE, W A; LETVIN, N; LI, J; SODROSKI, J
PA (DAND) DANA FARBER CANCER INST INC; (HARD) HARVARD COLLEGE
CYC 41
PI WO 9324632 A1 19931209 (199350)* EN 73
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AU BB BG BR CA CZ FI HU JP KR LK MG MN MW NO NZ PL RO RU SD
US
AU 9345223 A 19931230 (199415)
EP 642582 A1 19950315 (199515) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 08500965 W 19960206 (199643) 56
US 5654195 A 19970805 (199737) 19
ADT WO 9324632 A1 **WO 1993-US4814 19930520; AU 9345223 A AU 1993-45223
19930520; EP 642582 A1 EP 1993-915118 19930520, WO 1993-US4814
19930520; JP 08500965 W WO 1993-US4814 19930520, JP 1994-500637
19930520; US 5654195 A Cont of US 1992-887505 19920522, US 1994-2
19940701**
FDT AU 9345223 A Based on WO 9324632; EP 642582 A1 Based on WO 9324632
08500965 W Based on WO 9324632
PRAI US 1992-887505 19920522; US 1994-268799 19940701

L23 ANSWER 10 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1993-146253 [18] WPIDS
DNC C1993-065178
TI New oligo-deoxyribonucleoside phosphoro-thioate derivs. - are ant
oligo-nucleoside(s) active against HIV genes GAG, POL, VIF, VPR,
REV, ENV, NEF or LTR.
DC B04
PA (SAOK) SANYO KOKUSAKU PULP CO
CYC 1
PI JP 05078386 A 19930330 (199318)* 17
ADT JP 05078386 A **JP 1991-232339 19910820**
PRAI JP 1991-232339 19910820

L23 ANSWER 11 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1993-107741 [13] WPIDS
DNC C1993-047759
TI Concrete mixt. used in road construction - contains Portland ceme
water, coarse and fine filler and chemical additive to improve pro
DC A93 L02
IN AMINOV, E KH; GUSEV, B V; LITVAK, L A
PA (TSCA) TASHK CARS ROADS INST
CYC 1
PI SU 1726460 A1 19920415 (199313)* 5
ADT SU 1726460 A1 **SU 1990-4782421 19900116, SU 1990-4783489 19900116**
PRAI SU 1990-4782421 19900116; SU 1990-4783489 19900116

L23 ANSWER 12 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1993-065023 [08] WPIDS
DNN N1993-049595 DNC C1993-029292
TI Appts. for dosed feed of free flowing materials - contains drum w
longitudinal recesses as doser revolving under hopper discharge sl
determined conicity.
DC M23 P55
IN FILATOV, A I; KRASNOV, B P
PA (KRAS-I) KRASNOV B P
CYC 1
PI SU 1720822 A1 19920323 (199308)* 3
ADT SU 1720822 A1 **SU 1986-4034080 19860305**
PRAI SU 1986-4034080 19860305

L23 ANSWER 13 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1992-339475 [41] WPIDS
DNN N1992-258781
TI Method of measuring internal diameter of hollow electroconducting
from calibration characteristics taken at each frequency and from
amplitudes and phases of induced voltage.
DC S02
IN KASHAEV, YU G
PA (KASH-I) KASHAEV YU G
CYC 1
PI SU 1693364 A1 19911123 (199241)* 3
ADT SU 1693364 A1 **SU 1988-4416126 19880425**
PRAI SU 1988-4416126 19880425

L23 ANSWER 14 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1992-129926 [16] WPIDS
DNC C1992-061099
TI Rolled flat aluminium sheet plate and foil prodn. - includes mul

rolling at elevated temp. and calculated rolling rate.

DC M21 M29
 IN GORITSKOV, P N; SMAGORINSK, M E
 PA (LEKA) LENG D KALININ POLY
 CYC 1
 PI SU 1661241 A 19910707 (199216)* 3
 ADT SU 1661241 A **SU 1989-4699890 19890605**
 PRAI SU 1989-4699890 19890605

L23 ANSWER 15 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text
 AN 1992-056816 [07] WPIDS
 CR 1999-080408 [07]
 DNC C1992-025655
 TI Primate lentivirus vaccine protecting against AIDS - and primate
 lentiviruses and their DNA clones contg. null mutation(s), useful
 producing vaccine.
 DC B04 D16
 IN DESROSIERS, R C
 PA (HARD) HARVARD COLLEGE
 CYC 15
 PI WO 9200987 A 19920123 (199207)*
 RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
 W: JP
 EP 491930 A1 19920701 (199227) EN
 R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
 JP 05501654 W 19930402 (199318) 16
 EP 491930 B1 19970115 (199708) EN 20
 R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
 DE 69124215 E 19970227 (199714)
 ADT EP 491930 A1 **EP 1991-913715 19910710, WO 1991-US4884 19910710; JP**
05501654 W JP 1991-513074 19910710, WO 1991-US4884 19910710; EP 4
B1 EP 1991-913715 19910710, WO 1991-US4884 19910710; DE 69124215
1991-624215 19910710, EP 1991-913715 19910710, WO 1991-US4884 199
 FDT EP 491930 A1 Based on WO 9200987; JP 05501654 W Based on WO 920098
 491930 B1 Based on WO 9200987; DE 69124215 E Based on EP 491930, B
 WO 9200987
 PRAI US 1990-551945 19900712

L23 ANSWER 16 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text
 AN 1991-022239 [03] WPIDS
 DNC C1991-009577
 TI Vector contg. active **viral protein R** gene encoding protein - havi
 ability to trans-activate, useful for producing high levels of des
 heterologous gene prod..
 DC B04 D16
 IN COHEN, E; HASELTINE, W A; TERWILLIGE, E; TERWILLIGER, E
 PA (DAND) DANA FARBER CANCER INST INC
 CYC 15

PI WO 9015875 A 19901227 (199103)*
 RW: AT BE CH DE DK ES FR GB IT LU NL SE
 W: CA JP
 EP 474797 A 19920318 (199212) 39
 R: AT BE CH DE DK ES FR GB IT LI LU
 JP 04506605 W 19921119 (199301) 14
 EP 474797 A4 19920805 (199523)
 EP 474797 B1 19950906 (199540) EN
 R: AT BE CH DE DK ES FR GB IT LI LU NL SE
 DE 69022233 E 19951012 (199546)
 ADT EP 474797 A **EP 1990-915880 19900601**; JP 04506605 W **JP 1990-514932 19900601**, WO 1990-US3126 19900601; EP 474797 A4 EP 1990-915880
 ; EP 474797 B1 **EP 1990-915880 19900601**, WO 1990-US3126 19900601;
 69022233 E DE 1990-622233 19900601, EP 1990-915880 19900601, WO
 1990-US3126 19900601
 FDT JP 04506605 W Based on WO 9015875; EP 474797 B1 Based on WO 901587
 69022233 E Based on EP 474797, Based on WO 9015875
 PRAI US 1989-361028 19890602

L23 ANSWER 17 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text
 AN 1991-011155 [02] WPIDS
 DNN N1991-008418 DNC C1991-004938
 TI Negatively chargeable magnetic developer - has specified toner gr
 distribution, and provides image of high density.
 DC A89 E11 G08 P84 S06
 PA (CANO) CANON KK
 CYC 1
 PI JP 02284153 A 19901121 (199102)* 18
 JP 2728929 B2 19980318 (199816) 15
 ADT JP 02284153 A **JP 1989-106602 19890426**; JP 2728929 B2 **JP 1989-1066 19890426**
 FDT JP 2728929 B2 Previous Publ. JP 02284153
 PRAI JP 1989-106602 19890426

L23 ANSWER 18 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text
 AN 1990-378039 [51] WPIDS
 CR 1997-538622 [50]
 DNN N1990-288105 DNC C1990-164681
 TI New nucleotide sequences derived from genome of HIV-1, HIV-2 and
 useful as primers for amplification of immuno-deficiency viruses
 diagnosis and for raising antibodies in treatment of HIV infection
 DC B04 D16
 IN MONCANY, M; MONTAGNIER, L
 PA (INRM) INSERM INST NAT SANTE RE; (INSP) INST PASTEUR; (INRM) INSER
 NAT SANTE & RECH MEDICALE; (INRM) INST NAT SANTE & RECH MEDICALE
 CYC 17
 PI EP 403333 A 19901219 (199051)* 24
 R: AT BE CH DE ES FR GB GR IT LI LU NL SE

WO 9015066 A 19901213 (199101)
 W: CA JP US
 FR 2647809 A 19901207 (199105)#
 FR 2652091 A 19910322 (199121)
 JP 04507043 W 19921210 (199304)# 15
 WO 9015066 A3 19910418 (199508)
 US 5688637 A 19971118 (199801) 12
 EP 403333 B1 19991006 (199946) FR
 R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
 ES 2139567 T3 20000216 (200016)
 JP 2000093187 A 20000404 (200027) 14
 JP 3428012 B2 20030722 (200350) 23
 ADT EP 403333 A **EP 1990-401520 19900605; FR 2647809 A FR 1989-7354 19890602; FR 2652091 A FR 1989-12371 19890920; JP 04507043 W JP 1990-508911 19900605, WO 1990-FR393 19900605; WO 9015066 A3 WO 1990-FR393 19900605; US 5688637 A Cont of WO 1990-FR393 19900605, of US 1992-820599 19920121, US 1993-160465 19931202; EP 403333 B1 1990-401520 19900605, Related to EP 1997-110543 19900605; ES 2139 EP 1990-401520 19900605; JP 2000093187 A Div ex JP 1990-508911 19900605, JP 1999-270165 19900605; JP 3428012 B2 JP 1990-508911 19900605, WO 1990-FR393 19900605**
 FDT JP 04507043 W Based on WO 9015066; EP 403333 B1 Related to EP 8064 2139567 T3 Based on EP 403333; JP 3428012 B2 Previous Publ. JP 045 Based on WO 9015066
 PRAI FR 1989-12371 19890920; FR 1989-7354 19890602;
 JP 1990-508911 19900605

 L23 ANSWER 19 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text
 AN 1990-193937 [26] WPIDS
 DNC C1990-083913
 TI Microbial expression vectors - contg. viral protease gene to promo fusion protein cleavage.
 DC B04 D16
 IN KUBA, D
 PA (DEAK) AKAD WISSENSCHAFTEN DDR
 CYC 1
 PI DD 275259 A 19900117 (199026)*
 ADT DD 275259 A **DD 1988-319311 19880830**
 PRAI DD 1988-319311 19880830

 L23 ANSWER 20 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
 Full Text
 AN 1990-140772 [19] WPIDS
 DNN N1990-109156 DNC C1990-061793
 TI Negatively chargeable electrostatic developers - contains toner a hydrophobic silica fine powder made by treating silica with polysi amine cpd..
 DC A28 A89 G08 P84 S06
 IN KUKIMOTO, T

PA (CANO) CANON KK
CYC 6
PI DE 3933166 A 19900503 (199019)* 18
GB 2224582 A 19900509 (199019)
JP 02097967 A 19900410 (199020)
FR 2637390 A 19900406 (199021)
US 5043239 A 19910827 (199137) 12
GB 2224582 B 19920722 (199230)
JP 05029902 B 19930506 (199321) 11
IT 1237473 B 19930607 (199345)
DE 3933166 C2 19980416 (199819) 14
ADT DE 3933166 A DE 1989-3933166 19891004; GB 2224582 A GB 1989-22280 19891003; JP 02097967 A JP 1988-249744 19881005; FR 2637390 A FR 1989-12987 19891004; US 5043239 A US 1989-414292 19890929; GB 222 GB 1989-22280 19891003; JP 05029902 B JP 1988-249744 19881005; IT 1237473 B IT 1989-48429 19891005; DE 3933166 C2 DE 1989-3933166 1
FDT JP 05029902 B Based on JP 02097967
PRAI JP 1988-249744 19881005

L23 ANSWER 21 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1990-053071 [08] WPIDS
DNC C1990-022905
TI Amplifying nucleic acid sequences without cloning - by inserting into a vectorette and extension reacting at specific initiating pr region.
DC B04 D16
IN ANWAR, R; MARKHAM, A F; SMITH, J C
PA (ICIL) IMPERIAL CHEM IND PLC; (ZENE) ZENECA LTD
CYC 26
PI GB 2221909 A 19900221 (199008)*
EP 356021 A 19900228 (199009) EN
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
PT 91292 A 19900208 (199009)
NO 8903054 A 19900219 (199013)
BR 8903792 A 19900320 (199016)
DK 8903673 A 19900129 (199017)
FI 8903589 A 19900129 (199018)
ZA 8905473 A 19900328 (199018)
AU 8938966 A 19900322 (199032)
JP 02174679 A 19900706 (199033)
CN 1040220 A 19900307 (199049)
HU 53944 T 19901228 (199107)
DD 284053 A 19901031 (199114)
GB 2221909 B 19921111 (199246)
AU 635212 B 19930318 (199318)
IE 62579 B 19950405 (199522)
ADT GB 2221909 A GB 1989-17143 19890727; EP 356021 A EP 1989-307672 19890727; ZA 8905473 A ZA 1989-5473 19890718; JP 02174679 A JP 1989-196447 19890728; GB 2221909 B GB 1989-17143 19890727; AU 635

AU 1989-38966 19890725; IE 62579 B IE 1989-2307 19890717
FDT AU 635212 B Previous Publ. AU 8938966
PRAI GB 1988-18020 19880728; GB 1989-17143 19890727

L23 ANSWER 22 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 1989-217600 [30] WPIDS

DNN N1989-165652 DNC C1989-097030

TI Hot working of titanium ingots - by applying working strain on ing
surface, heating to above recrystallisation temp. and hot-working

DC M29 P51

PA (YAWA) NIPPON STEEL CORP

CYC 1

PI JP 01156456 A 19890620 (198930)* 4

ADT JP 01156456 A JP 1987-313682 19871211

PRAI JP 1987-313682 19871211

L23 ANSWER 23 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 1989-152803 [21] WPIDS

DNN N1989-116588

TI Electrical drive circuit for inductive load e.g. coils of vibrator
includes device to compare energisation signal and reference signal
generate error signal.

DC P43 V06 X25

IN PARDOE, B H; BEVERLY, H PARDOE

PA (BRTE-N) BRITISH TECHNOLOGY GROUP LTD; (NATR) NAT RES DEV CORP

CYC 6

PI EP 317333 A 19890524 (198921)* EN 6

R: CH DE FR GB LI

GB 2213293 A 19890809 (198932)

GB 2213293 B 19920318 (199212)

US 5130618 A 19920714 (199231) 6

EP 317333 B1 19970212 (199712) EN 8

R: CH DE FR GB LI

DE 3855794 G 19970327 (199718)

ADT EP 317333 A EP 1988-310900 19881118; GB 2213293 A GB 1988-27042
19881118; GB 2213293 B GB 1988-27042 19881118; US 5130618 A Cont
1988-273351 19881118, US 1989-455915 19891228; EP 317333 B1 EP
1988-310900 19881118; DE 3855794 G DE 1988-3855794 19881118, EP
1988-310900 19881118

FDT DE 3855794 G Based on EP 317333

PRAI GB 1987-27070 19871119; GB 1988-27042 19881118

L23 ANSWER 24 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 1988-290808 [41] WPIDS

DNC C1988-129295

TI Determn. of microorganism concn. in suspension by microscopy - in
immuno-fluorescent analysis of suspension fixed in polymeric gel,

increase reliability and reduce time.

DC A89 D16 J04

IN MATYSYAK, M A; OLENEV, V I

PA (BIOL-R) BIOL INSTRMN RES

CYC 1

PI SU 1382848 A 19880323 (198841)* 4

ADT SU 1382848 A SU 1986-4114593 19860908

PRAI SU 1986-4114593 19860908

L23 ANSWER 25 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

Full Text

AN 1987-221261 [31] WPIDS

CR 1987-329355 [47]; 1988-149264 [22]; 1988-220290 [31]; 1988-272808
1992-041067 [05]; 2000-328365 [28]; 2002-434814 [46]; 2003-553960
2004-070575 [07]

DNN N1987-165620 DNC C1987-093098

TI New type of human immuno-deficiency virus, infections for T4 cells
derived antigens, immunogens, monoclonal antibodies and nucleic ac
sequences, e.g. for diagnosis of AIDS.

DC B04 D16 S03

IN ALIZON, M; BRUN-VEZINET, F; CHAMARET, S; CLAVEL, F; GUETARD, D; GU
M; KATLAMA, C; MONTAGNIER, L; REY, M; ROUZIOUX, C; SONIGO, P; BRUN
F; ROUXIOUX, C; SOLANGE, C; GEUTARD, D; DUETARD, D; GUETARD, D G;
BURNVEZINE, F

PA (INSP) INST PASTEUR; (ALIZ-I) ALIZON M; (BRUN-I) BRUN-VEZINET F;
CLAVEL F; (GUET-I) GUETARD D; (MONT-I) MONTAGNIER L

CYC 24

PI WO 8704459 A 19870730 (198731)* FR 116

RW: OA

W: AU DK JP KR US

FR 2593189 A 19870724 (198736)

FR 2593190 A 19870724 (198736)

FR 2593922 A 19870807 (198738)

EP 239425 A 19870930 (198739) FR 164

R: AT BE CH DE ES FR GB GR IT LI LU NL SE

FR 2594229 A 19870814 (198739)

AU 8768911 A 19870814 (198743)

FR 2596063 A 19870925 (198743)

ZA 8700469 A 19870714 (198744)

FR 2597500 A 19871023 (198750)

PT 84182 A 19880122 (198809)

DK 8704934 A 19871117 (198827)

JP 63502242 W 19880901 (198841)

EP 320495 A 19890614 (198924) FR

R: AT BE CH DE ES FR GB GR IT LI LU NL SE

US 4839288 A 19890613 (198930) 8

EP 239425 B 19891102 (198944) FR

R: AT BE CH DE ES FR GB GR IT LI LU NL SE

DE 3760912 G 19891207 (198950)

ES 2013295 B 19900501 (199023)

US 5030718	A	19910709	(199130)	
US 5051496	A	19910924	(199141)	
US 5055391	A	19911008	(199143)	
US 5066782	A	19911119	(199149)	
US 5268265	A	19931207	(199350) #	
US 5306614	A	19940426	(199416)	32
US 5310651	A	19940510	(199418)	15
JP 06113833	A	19940426	(199421)	34
US 5364933	A	19941115	(199445)	7
JP 07233196	A	19950905	(199544)	27
JP 08113598	A	19960507	(199628)	28
CA 1338323	C	19960514	(199629)	
US 5545726	A	19960813	(199638)	14
JP 08275783	A	19961022	(199701)	29
US 5578715	A	19961126	(199702)	18
US 5580739	A	19961203	(199703)	42
US 5597896	A	19970128	(199710)	7
JP 09037778	A	19970210	(199716)	27
JP 09075092	A	19970325	(199722)	27
JP 2611106	B2	19970521	(199725)	48
JP 2735521	B2	19980402	(199818)	28
JP 2771519	B2	19980702	(199831)	27
US 5770703	A	19980623	(199832)	
JP 2801162	B2	19980921	(199843)	30
MX 185326	A	19970718	(199846)	
US 5830641	A	19981103	(199851)	
US 5866319	A	19990202	(199912)	
JP 11018768	A	19990126	(199914)	29
JP 2865203	B2	19990308	(199915)	33
JP 2874846	B2	19990324	(199917)	33
US 5889158	A	19990330	(199920)	
JP 2931294	B2	19990809	(199937)	28
US 5976785	A	19991102	(199953)	
US 6037165	A	20000314	(200020)	
US 6048685	A	20000411	(200025)	
EP 320495	B1	20000802	(200038) # FR	
R: AT BE CH DE ES FR GB GR IT LI LU NL SE				
DE 3752319	G	20000907	(200044)	
US 6162439	A	20001219	(200102)	
ES 2150897	T3	20001216	(200105)	
US 6261762	B1	20010717	(200142)	
US 6265149	B1	20010724	(200146)	
US 6296807	B1	20011002	(200160)	
US 6316183	B1	20011113	(200173)	
US 6355789	B1	20020312	(200221)	
US 6429306	B1	20020806	(200254)	
US 6514691	B1	20030204	(200313)	
US 6518015	B1	20030211	(200314)	
US 2003082523	A1	20030501	(200331)	
US 2003091985	A1	20030515	(200335)	

US 2003186219 A1 20031002 (200365)
 US 2003170658 A1 20030911 (200367)
 IE 83207 B 20031210 (200381)
 US 6664041 B2 20031216 (200382)
 ADT WO 8704459 A WO 1987-FR25 19870122; FR 2593189 A FR 1986-910 1986
 FR 2593190 A FR 1986-911 19860122; FR 2593922 A FR 1986-1635 1986
 EP 239425 A EP 1987-400151 19870122; FR 2594229 A FR 1986-1985
 19860213; FR 2596063 A FR 1986-3881 19860318; ZA 8700469 A ZA 198
 19870122; FR 2597500 A FR 1986-4215 19860324; JP 63502242 W JP
 1987-500920 19870122; EP 320495 A Div ex EP 1987-400151 19870122,
 1989-101328 19870122; US 4839288 A US 1986-835228 19860303; US 50
 A US 1990-462984 19900110; US 5051496 A US 1987-3764 19870116; US
 5055391 A US 1990-462353 19900103; US 5066782 A US 1990-462908
 19900110; US 5268265 A Div ex US 1986-835228 19860303, Cont of US
 1988-273050 19881118, US 1991-703048 19910517; US 5306614 A CIP o
 1986-835228 19860303, CIP of US 1986-916080 19861006, CIP of US
 1986-933184 19861121, CIP of US 1987-3764 19870116, Div ex US
 1987-13477 19870211, Div ex US 1991-752368 19910903, US 1991-8108
 19911220; US 5310651 A CIP of US 1986-835228 19860303, Cont of US
 1986-916080 19861006, Cont of US 1986-933184 19861121, Cont of US
 1990-602383 19901024, Cont of US 1990-604323 19901024, US 1991-75
 19910909; JP 06113833 A Div ex JP 1987-500920 19870122, JP 1993-1
 19870122; US 5364933 A Div ex US 1986-835228 19860303, Cont of US
 1989-365117 19890612, Cont of US 1991-771893 19911007, Div ex US
 1992-911364 19920713, US 1992-929432 19920814; JP 07233196 A Div
 1993-12972 19870122, JP 1994-329070 19870122; JP 08113598 A Div e
 1993-12972 19870122, JP 1995-257991 19870122; CA 1338323 C CA
 1987-529362 19870210; US 5545726 A CIP of US 1986-835228 19860303
 of US 1986-916080 19861006, Cont of US 1986-933184 19861121, Cont
 US 1990-602383 19901024, Cont of US 1990-604323 19901024, Cont of
 1991-756998 19910910, US 1993-132919 19931007; JP 08275783 A Div
 1993-12972 19870122, JP 1996-33969 19870122; US 5578715 A CIP of
 1986-835228 19860303, CIP of US 1986-916080 19861006, CIP of US
 1986-933184 19861121, Div ex US 1987-3764 19870116, US 1991-75490
 19910904; US 5580739 A CIP of US 1986-835228 19860303, CIP of US
 1986-916080 19861006, CIP of US 1986-933184 19861121, CIP of US
 1987-3764 19870116, Div ex US 1987-13477 19870211, Div ex US
 1991-752368 19910903, Div ex US 1991-810908 19911220, US 1994-214
 19940317; US 5597896 A Div ex US 1986-835228 19860303, Cont of US
 1989-365117 19890612, Cont of US 1991-771893 19911007, Div ex US
 1992-911364 19920713, Div ex US 1992-929432 19920814, US 1994-202
 19940225; JP 09037778 A Div ex JP 1994-329070 19870122, JP 1996-1
 19870122; JP 09075092 A Div ex JP 1987-500920 19870122, JP 1995-2
 19870122; JP 2611106 B2 Div ex JP 1987-500920 19870122, JP 1993-1
 19870122; JP 2735521 B2 Div ex JP 1987-500920 19870122, JP 1995-2
 19870122; JP 2771519 B2 Div ex JP 1994-329070 19870122, JP 1996-1
 19870122; US 5770703 A CIP of US 1986-835228 19860303, CIP of US
 1986-916080 19861006, CIP of US 1986-933184 19861121, CIP of US
 1987-3764 19870116, Div ex US 1987-13477 19870211, Div ex US
 1991-752368 19910903, Div ex US 1991-810908 19911220, Cont of US

1994-214221 19940317, US 1995-468774 19950606; JP 2801162 B2 Div
1993-12972 19870122, JP 1995-257991 19870122; MX 185326 A MX
1987-26941 19870122; US 5830641 A CIP of US 1986-835228 19860303,
of US 1986-916080 19861008, CIP of US 1986-933184 19861121, CIP o
1987-3764 19870116, Cont of WO 1987-FR25 19870122, Cont of US
1987-150645 19871120, Div ex US 1990-462908 19900110, Cont of US
1991-792524 19911118, Div ex US 1993-75020 19930611, US 1994-2142
19940317; US 5866319 A CIP of US 1986-835228 19860303, CIP of US
1986-916080 19861006, CIP of US 1986-933184 19861121, Div ex US
1987-3764 19870116, Cont of US 1991-754903 19910904, US 1995-4680
19950606; JP 11018768 A Div ex JP 1995-257991 19870122, JP 1998-1
19870122; JP 2865203 B2 JP 1987-500920 19870122, WO 1987-FR25
19870122; JP 2874846 B2 Div ex JP 1987-500920 19870122, JP 1996-3
19870122; US 5889158 A Div ex US 1986-835228 19860303, Cont of US
1989-365117 19890612, Cont of US 1991-771893 19911007, Div ex US
1992-911364 19920713, Div ex US 1992-929432 19920814, Cont of US
1994-202260 19940225, US 1995-466704 19950606; JP 2931294 B2 Div
1995-257991 19870122, JP 1998-119235 19870122; US 5976785 A CIP o
1986-835228 19860303, CIP of US 1986-916080 19861006, CIP of US
1986-933184 19861121, CIP of US 1987-3764 19870116, Div ex US
1987-13477 19870211, Div ex US 1991-752368 19910903, US 1991-8111
19911220; US 6037165 A CIP of US 1986-835228 19860303, CIP of US
1986-916080 19861006, CIP of US 1986-933184 19861121, CIP of US
1987-3764 19870116, Cont of US 1987-150645 19871120, Div ex US
1990-462908 19900110, Cont of US 1991-792524 19911118, Cont of US
1993-75020 19930611, Div ex US 1995-392613 19950222, US 1995-4704
19950606; US 6048685 A CIP of US 1986-835228 19860303, CIP of US
1986-916080 19861006, CIP of US 1986-933184 19861121, CIP of US
1987-3764 19870116, Div ex US 1987-13477 19870211, Div ex US
1991-752368 19910903, Cont of US 1991-810908 19911220, US 1995-46
19950606; EP 320495 B1 Div ex EP 1987-400151 19870122, EP 1989-10
19870122; DE 3752319 G DE 1987-3752319 19870122, EP 1989-101328
19870122; US 6162439 A CIP of US 1986-835228 19860303, CIP of US
1986-916080 19861006, CIP of US 1986-933184 19861121, CIP of US
1987-3764 19870116, Div ex US 1987-13477 19870211, Div ex US
1991-752368 19910903, Cont of US 1991-810908 19911220, US 1995-46
19950606; ES 2150897 T3 EP 1989-101328 19870122; US 6261762 B1 CI
US 1986-835228 19860303, CIP of US 1986-916080 19861006, CIP of U
1986-931866 19861121, CIP of US 1986-933184 19861121, CIP of US
1987-3764 19870116, Div ex US 1987-13477 19870211, Div ex US
1991-752368 19910903, Cont of US 1991-810908 19911220, US 1997-77
19970102; US 6265149 B1 CIP of US 1986-835228 19860303, CIP of US
1986-916080 19861006, CIP of US 1986-933184 19861121, CIP of US
1987-3764 19870116, Cont of US 1987-150645 19871120, Div ex US
1990-462908 19900110, Cont of US 1991-792524 19911118, Cont of US
1993-75020 19930611, Div ex US 1995-392613 19950222, US 1995-4704
19950606; US 6296807 B1 Div ex US 1986-835228 19860303, Cont of U
1989-365117 19890612, Cont of US 1991-771893 19911007, Div ex US
1992-911364 19920713, Div ex US 1992-929432 19920814, Cont of US
1994-202260 19940225, Div ex US 1995-466704 19950606, US 1998-143

19980828; US 6316183 B1 CIP of US 1986-835228 19860303, Cont of U
 1986-916080 19861006, Cont of US 1986-933184 19861121, Cont of US
 1990-602383 19901024, Cont of US 1990-604323 19901024, Cont of US
 1991-756998 19910909, Cont of US 1993-132919 19931007, US 1995-46
 19950606; US 6355789 B1 CIP of US 1986-835228 19860303, CIP of US
 1986-916080 19861006, CIP of US 1986-933184 19861121, CIP of US
 1987-3764 19870116, Div ex US 1987-13477 19870211, Div ex US
 1991-752368 19910903, Div ex US 1991-810908 19911220, Cont of US
 1994-214221 19940317, US 1995-468424 19950606; US 6429306 B1 CIP
 1986-835228 19860303, CIP of US 1986-916080 19861006, CIP of US
 1986-933184 19861121, CIP of US 1987-3764 19870116, Cont of WO
 1987-FR25 19870122, Cont of US 1987-150645 19871120, Div ex US
 1990-462908 19900110, Cont of US 1991-792524 19911118, Cont of US
 1993-75020 19930611, US 1995-392613 19950222; US 6514691 B1 CIP o
 1986-835228 19860303, CIP of US 1986-916080 19861006, CIP of US
 1986-933184 19861121, Div ex US 1987-3764 19870116, Cont of US
 1991-754903 19910904, Cont of US 1995-468093 19950606, US 1998-19
 19981113; US 6518015 B1 CIP of US 1986-835228 19860303, CIP of US
 1986-916080 19861006, CIP of US 1986-933184 19861121, Div ex US
 1987-3764 19870116, Div ex US 1987-13477 19870211, Div ex US
 1991-752368 19910903, Div ex US 1991-810908 19911220, Cont of US
 1997-774736 19970102, US 2000-862029 20000512; US 2003082523 A1 C
 1986-835228 19860303, CIP of US 1986-916080 19861006, CIP of US
 1986-933184 19861121, Div ex US 1987-3764 19870116, Cont of US
 1991-754903 19910904, Cont of US 1995-468093 19950606, Div ex US
 1998-191384 19981113, US 2002-133357 20020429; US 2003091985 A1 C
 1986-835228 19860303, CIP of US 1986-916080 19861006, CIP of US
 1986-933184 19861121, CIP of US 1987-3764 19870116, Div ex US
 1987-13477 19870211, Div ex US 1991-752368 19910903, Div ex US
 1991-810908 19911220, Cont of US 1994-214221 19940317, Cont of US
 1995-468424 19950606, US 2001-988213 20011119; US 2003186219 A1 C
 1986-835228 19860303, CIP of US 1986-916080 19861006, Cont of US
 1986-916080 19861006, Cont of US 1986-933184 19861121, Cont of US
 1990-602383 19901024, Cont of US 1991-756998 19910909, Cont of US
 1993-132919 19931007, Cont of US 1995-467161 19950606, US 2001-98
 20011109; US 2003170658 A1 CIP of US 1986-835228 19860303, CIP of
 1986-916080 19861006, CIP of US 1986-933184 19861121, CIP of US
 1987-3764 19870116, Cont of US 1987-150645 19871120, Div ex US
 1990-462908 19900110, Cont of US 1991-792524 19911118, Cont of US
 1993-75020 19930611, Cont of US 1995-392613 19950222, Div ex US
 1995-470491 19950606, Div ex US 2001-862511 20010523, US 2002-180
 20020627; IE 83207 B IE 1987-174 19870122; US 6664041 B2 CIP of U
 1986-835228 19860303, CIP of US 1986-916080 19861006, CIP of US
 1986-933184 19861121, CIP of US 1987-3764 19870116, Cont of US
 1987-150645 19871120, Div ex US 1990-462908 19900110, Cont of US
 1991-792524 19911118, Cont of US 1993-75020 19930611, Cont of US
 1995-392613 19950222, Div ex US 1995-470491 19950606, US 2001-862
 20010523

FDT US 5268265 A Div ex US 4839288; US 5306614 A CIP of US 4839288, Di
 5079342; US 5310651 A CIP of US 4839288; US 5364933 A Div ex US 48

US 5545726 A CIP of US 4839288, Cont of US 5310651; US 5578715 A C 4839288, Div ex US 5051496; US 5580739 A CIP of US 4839288, CIP of 5051496, Div ex US 5079342; US 5597896 A Div ex US 4839288, Div ex 5364933; JP 2611106 B2 Previous Publ. JP 06113833; JP 2735521 B2 P Publ. JP 09075092; JP 2771519 B2 Previous Publ. JP 09037778; US 57 CIP of US 4839288, CIP of US 5051496, Div ex US 5079342; JP 280116 Previous Publ. JP 08113598; US 5830641 A CIP of US 4839288, CIP of 5051496, Div ex US 5066782; US 5866319 A CIP of US 4839288, Div ex 5051496, Cont of US 5578715; JP 2865203 B2 Previous Publ. JP 63502 Based on WO 8704459; JP 2874846 B2 Previous Publ. JP 08275783; US A Div ex US 4839288, Div ex US 5364933, Cont of US 5597896; JP 293 Previous Publ. JP 11018768; US 5976785 A CIP of US 4839288, CIP of 5051496, Div ex US 5079342; US 6037165 A CIP of US 4839288, CIP of 5051496, Div ex US 5066782; US 6048685 A CIP of US 4839288, CIP of 5051496, Div ex US 5079342; EP 320495 B1 Div ex EP 239425; DE 3752 Based on EP 320495; US 6162439 A CIP of US 4839288, CIP of US 5051 ex US 5079342; ES 2150897 T3 Based on EP 320495; US 6261762 B1 CIP 4839288, CIP of US 5051496, Div ex US 5079342; US 6265149 B1 CIP o 4839288, CIP of US 5051496, Div ex US 5066782; US 6296807 B1 Div e 4839288, Div ex US 5364933, Cont of US 5597896, Div ex US 5889158; 6316183 B1 CIP of US 4839288, Cont of US 5310651, Cont of US 55457 6355789 B1 CIP of US 4839288, CIP of US 5051496, Div ex US 5079342 of US 5580739; US 6429306 B1 CIP of US 4839288, CIP of US 5051496, US 5066782; US 6514691 B1 CIP of US 4839288, Div ex US 5051496, Co 5578715, Cont of US 5866319; US 6518015 B1 CIP of US 4839288, Div 5051496, Div ex US 5079342, Cont of US 6261762; US 2003082523 A1 C 4839288, Div ex US 5051496, Cont of US 5578715, Cont of US 5866319 2003091985 A1 CIP of US 4839288, CIP of US 5051496, Div ex US 5079 Cont of US 5580739, Cont of US 6355789; US 2003170658 A1 CIP of US 4839288, CIP of US 5051496, Div ex US 5066782, Div ex US 6265149, US 6429306; US 6664041 B2 CIP of US 4839288, CIP of US 5051496, Di 5066782, Div ex US 6265149, Cont of US 6429306

PRAI US 1987-13477	19870211; FR 1986-910	19860122;
FR 1986-911	19860122; FR 1986-1635	19860206;
FR 1986-1985	19860213; US 1986-835228	19860303;
FR 1986-3881	19860318; FR 1986-4215	19860324;
US 1986-916080	19861006; US 1986-933184	19861121;
EP 1987-400151	19870122; EP 1989-101328	19870122;
US 1990-462984	19900110; US 1987-3764	19870116;
US 1990-462353	19900103; US 1990-462908	19900110;
US 1991-703048	19910517; US 1989-365117	19890612;
US 1991-771893	19911007; US 1992-911364	19920713;
US 1992-929432	19920814; US 1986-931866	19861121;
US 1997-774736	19970102; FR 1986-4556	19860328

L23 ANSWER 26 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN Full Text

AN 1987-197261 [28] WPIDS

DNN N1987-147393 DNC C1987-082810

TI Brazing graphite ring in titanium cylinder - by two-stage heating

vacuum and cooling in furnace to 700 deg. C followed by slow cooli
DC A81 M23 P55
IN PEREVESENT, B N; SHISHKINA, R N; SOKOLOVA, N M
PA (TOLY-R) TOLYATIN POLY
CYC 1
PI SU 1271694 A 19861123 (198728)* 3
ADT SU 1271694 A **SU 1985-3934499 19850726**
PRAI SU 1985-3934499 19850726

L23 ANSWER 27 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1987-008860 [02] WPIDS
TI Low temp. resistant mouldings from amide blends with graft copolym
obtd. by grafting elastomers with mono isocyanate adducts of hydro
(meth)acrylate(s).
DC A18 A23
IN BARTL, H; LINDNER, C; OTT, K H; SULING, C; TRABERT, L; WITTMANN, D
PA (FARB) BAYER AG
CYC 8
PI EP 208187 A 19870114 (198702)* GE
R: DE FR GB IT NL SE
DE 3524234 A 19870108 (198702)
JP 62013421 A 19870122 (198709)
US 4873289 A 19891010 (198950) 6
EP 208187 B 19901107 (199045)
R: DE FR GB IT NL SE
DE 3675440 G 19901213 (199051)
ADT EP 208187 A **EP 1986-108515 19860623**; DE 3524234 A **DE 1985-3524234**
19850706; JP 62013421 A **JP 1986-154270 19860702**; US 4873289 A **US**
1988-246887 19880915
PRAI DE 1985-3524234 19850706

L23 ANSWER 28 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1986-107516 [17] WPIDS
DNC C1986-045908
TI Vinyl propionate copolymer aq. emulsions prepn. - for paint and p
binders, by emulsion copolymerisation with T-butyl acrylate, (met
acid and unsatd. carboxylate.
DC A14 A82 A93 G02 L02
IN KERCKOW, A; MATTHAI, L; PETERS, K C; WISTUBA, E
PA (BADI) BASF AG
CYC 1
PI DE 3437920 A 19860417 (198617)* 9
DE 3437920 C 19890406 (198914)
ADT DE 3437920 A **DE 1984-3437920 19841017**
PRAI DE 1984-3437920 19841017

L23 ANSWER 29 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 1983-759874 [37] WPIDS
DNN N1983-160449
TI Light type selector - is for camera which is set automatically for daylight if electronic flash is primed.
DC P82 S06 W04
IN MURAMOTO, T; NISHIMURA, A; TAKAYMA, M
PA (CANO) CANON KK
CYC 3
PI DE 3306705 A 19830908 (198337)* 27
JP 58147721 A 19830902 (198341)
US 4499487 A 19850212 (198509)
US 4567509 A 19860128 (198607)
JP 61216585 A 19860926 (198645)
DE 3306705 C 19920409 (199215) 11
ADT JP 58147721 A JP 1985-20502 ; US 4499487 A US 1983-467348
19830217; US 4567509 A US 1984-652171 19840918
PRAI JP 1982-31228 19820226; JP 1986-20502 19820302

L23 ANSWER 30 OF 30 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 1982-P1133E [43] WPIDS
TI Large scale integrated semiconductor memory - has fault detection circuits, each with bistable multivibrator, to switch data from fa cells to reserve cells.
DC T01 U14
IN YAMADA, J
PA (NITE) NIPPON TELEGRAPH & TELEPHONE CORP
CYC 6
PI NL 8200978 A 19821001 (198243)* 28
FR 2501891 A 19820917 (198244)
GB 2097621 A 19821103 (198244)
DE 3208763 A 19821104 (198301)
US 4460998 A 19840717 (198431)
CA 1172768 A 19840814 (198437)
GB 2097621 B 19850703 (198527)
ADT GB 2097621 A GB 1982-6917 19820309; US 4460998 A US 1982-356041 1
PRAI JP 1981-34799 19810311

=> file uspatful

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	196.00	369.05

FILE 'USPATFULL' ENTERED AT 08:27:37 ON 04 APR 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 31 Mar 2005 (20050331/PD)
FILE LAST UPDATED: 31 Mar 2005 (20050331/ED)
HIGHEST GRANTED PATENT NUMBER: US6874161

HIGHEST APPLICATION PUBLICATION NUMBER: US2005071904
CA INDEXING IS CURRENT THROUGH 31 Mar 2005 (20050331/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 31 Mar 2005 (20050331/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2005

>>> USPAT2 is now available. USPATFULL contains full text of the
>>> original, i.e., the earliest published granted patents or
>>> applications. USPAT2 contains full text of the latest US
>>> publications, starting in 2001, for the inventions covered in
>>> USPATFULL. A USPATFULL record contains not only the original
>>> published document but also a list of any subsequent
>>> publications. The publication number, patent kind code, and
>>> publication date for all the US publications for an invention
>>> are displayed in the PI (Patent Information) field of USPATFULL
>>> records and may be searched in standard search fields, e.g., /PN,
>>> /PK, etc.

>>> USPATFULL and USPAT2 can be accessed and searched together
>>> through the new cluster USPATALL. Type FILE USPATALL to
>>> enter this cluster.
>>>
>>> Use USPATALL when searching terms such as patent assignees,
>>> classifications, or claims, that may potentially change from
>>> the earliest to the latest publication.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s us6706268/pn
L24 1 US6706268/PN

=> d l24,cbib,ab,clm

L24 ANSWER 1 OF 1 USPATFULL on STN
2004:65817 Human deficiency virus type-1 (HIV-1) peptide encoded by th
gene.
Alizon, Marc, Paris, FRANCE
Sonigo, Pierre, Paris, FRANCE
Stewart, Cole, Chatillon, FRANCE
Danos, Oliver, Paris, FRANCE
Wain-Hobson, Simon, Montigny les Bretonneux, FRANCE
Institut Pasteur, Paris, FRANCE (non-U.S. corporation)Centre Nation
Recherche Scientifique, Paris, FRANCE (non-U.S. corporation)
US 6706268 B1 20040316 <-
APPLICATION: US 2000-709316 20001113 (9)
PRIORITY: FR 1984-16013 19841018
GB 1984-29099 19841116
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention is in the field of lymphadenopathy virus. This invention relates to a diagnostic means and method to detect the presence of RNA or antibodies of the lymphadenopathy retrovirus associated with acquired immune deficiency syndrome or of the lymphadenopathy syndrome by the use of DNA fragments or the peptides encoded by said DNA fragments. The invention further relates to the DNA fragments, comprising them and the proteins expressed.

CLM What is claimed is:

1. A purified peptide encoded by the vpr gene of HIV-1, wherein the peptide is free of particles of said virus and has the following acid sequence: Met-Glu-Ala-Pro-Glu-Asp-Gln-Gly-Pro-Gln-Arg-Asp-Asn-Glu-Trp-Thr-Leu-Gln-Leu-Leu-Glu-Glu-Leu-Lys-Asn-Glu-Ala-Val-Phe-Pro-Arg-Ile-Trp-Leu-His-Gly-Leu-Gly-Gln-His-Ile-Tyr-Glu-Thr-Asp-Thr-Trp-Ala-Gly-Val-Glu-Ala-Ile-Ile-Arg-Ile-Leu-Gln-Gln-Leu-Ile-His-Phe-Arg-Ile-Gly-Cys-Arg-His-Ser-Arg-Ile-Gly-Val-Thr-Gln-Arg-Ala-Arg-Asn-Gly-Ala-Ser-Arg-Ser.

2. A peptide of HIV-1 expressed from DNA corresponding to the vpr reading frame, the DNA having the following nucleotide sequence:

```
5030      5040      5050      5060      5070
  AT GGAACAAGCC CCAGAAGACC AAGGGCCACA GAGGGAGCCA

      5080      5090      5100      5110      5120
 CACAAGTAAG GGACACTAGA GCTTTTAGAG GAGCTTAAGA ATGAAGCTGT

      5130      5140      5150      5160      5170
 TAGACATTTT CCTAGGATTT GGCTCCATGG CTTAGGGCAA CATATCTATG

      5180      5190      5200      5210      5220
 AAACTTATGG GGATACTTGG GCAGGAGTGG AAGCCATAAT AAGAATTCTG

      5230      5240      5250      5260      5270
 CAACAAC TGC TGTTTATCCA TTTCAGAATT GGGTGTCGAC ATAGCAGAAT

      5280      5290      5300      5310
 AGGCGTTACT CAACAGAGGA GAGCAAGAAA TGGAGCCAGT AGATCC, wherein the
 recombinant DNA molecule.
```

=> file medline

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION

FULL ESTIMATED COST

7.08	376.13
------	--------

FILE 'MEDLINE' ENTERED AT 08:29:34 ON 04 APR 2005

FILE LAST UPDATED: 2 APR 2005 (20050402/UP). FILE COVERS 1950 TO DATE

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s (HIV or human immunodeficiency virus)
    145894 HIV
    1246766 HUMAN
    117491 IMMUNODEFICIENCY
    391165 VIRUS
    45423 HUMAN IMMUNODEFICIENCY VIRUS
        (HUMAN(W) IMMUNODEFICIENCY(W) VIRUS)
L25    150879 (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
```

```
=> s l25 and (Vpr or viral protein R)
    823 VPR
    326449 VIRAL
    1379612 PROTEIN
    261267 R
    62 VIRAL PROTEIN R
        (VIRAL(W) PROTEIN(W) R)
L26    677 L25 AND (VPR OR VIRAL PROTEIN R)
```

```
=> s l26 and (Vpr/ab or viral protein R/ab)
    716 VPR/AB
    113277 VIRAL/AB
    909138 PROTEIN/AB
    227742 R/AB
    53 VIRAL PROTEIN R/AB
        ((VIRAL(W) PROTEIN(W) R)/AB)
L27    606 L26 AND (VPR/AB OR VIRAL PROTEIN R/AB)
```

```
=> s l27 and py<1994
    9797716 PY<1994
L28    55 L27 AND PY<1994
```

```
=> d l28,cbib,ab,25-55
```

```
L28  ANSWER 25 OF 55      MEDLINE on STN
92068103.  PubMed ID: 1835572.  Human immunodeficiency virus type 1
```

vif, **vpr**, and vpu mutants can produce persistently infected cells. Nishino Y; Kishi M; Sumiya M; Ogawa K; Adachi A; Maotani-Imai K; Hirai K; Ikuta K. (Institute of Immunological Science, Hokkaido University, Japan.) Archives of virology, (1991) 120 (3-4) 181-9 Journal code: 7506870. ISSN: 0304-8608. Pub. country: Austria. Lan English.

AB A series of **human immunodeficiency virus** type 1 (**HIV-1**) mutants i vif, **vpr**, vpu, and nef were constructed from an infectious plasmid 432) containing the full-length **HIV-1** DNA by frameshift mutations. capacities for replication and cell killing of these mutant virus examined in a clonal cell line (M 10) isolated from HTLV-I-transf MT-4 cells. In all cases, the mutant viruses replicated, expresse **HIV-1** antigens, and induced drastic cytopathic effects. However, 10 cells survived infection with vif, **vpr**, and vpu mutant viruses became persistently **HIV-1**-infected, whereas no cells survived infe with the nef mutant as well as the wild-type virus. The **HIV-1** pa produced from the surviving cells after infection with the vif, v vpu mutant viruses were fully replicative in M 10 cells without ap cytopathic effects.

L28 ANSWER 26 OF 55 MEDLINE on STN
92024082. PubMed ID: 1926777. Analysis of alternatively spliced h **immunodeficiency virus** type-1 mRNA species, one of which encodes a novel tat-env fusion protein. Furtado M R; Balachandran R; Gupta P Wolinsky S M. (Department of Medicine, Northwestern University Med School, Chicago, Illinois 60611.) Virology, (1991 Nov) 185 (1) 2 Journal code: 0110674. ISSN: 0042-6822. Pub. country: United State Language: English.

AB A polymerase chain reaction-based analysis was used to define the structures of the mRNAs that encode **human immunodeficiency virus** type-1 (**HIV-1**) regulatory and structural proteins in infected H9 c Twenty alternatively spliced mRNAs encoding the vif, **vpr**, env, ne and rev proteins were characterized. An evaluation of the coding potentials of these transcripts recognized both leaky scanning and reinitiation at downstream initiation codons as mechanisms that ma operate during translation of many of the polycistronic messages. splice acceptor sites, one at nt 6018 defining a new mRNA coding f env and vpu proteins and another at nt 8671 defining a novel tat-fusion transcript, were characterized. The latter transcript expr novel protein p17tev that was immunoprecipitated by both polyclona antibodies and monoclonals directed towards the C-terminal region The p17tev protein was able to transactivate transcription from th **HIV-1** LTR in transient transfection assays. The use of multiple alternative splice donor and acceptor sites and the generation of proteins may confer evolutionary advantages on the viral mutants e them and influence the course of clinical disease.

L28 ANSWER 27 OF 55 MEDLINE on STN
91359921. PubMed ID: 1886517. Genetic regulation of **human immunodeficiency virus**. Steffy K; Wong-Staal F. (Department of

Medicine, University of California, San Diego, La Jolla 92093.) Microbiological reviews, (1991 Jun) 55 (2) 193-205. Ref: 123. Jo code: 7806086. ISSN: 0146-0749. Pub. country: United States. Langu English.

AB **Human immunodeficiency virus (HIV)** has a complex life cycle in which both cellular and virus-encoded factors participate to deter level of virus production. Two of the viral genes, *tat* and *rev*, a essential for virus replication and encode novel trans-activators interact specifically with their cognate RNA target elements. Elu of their mechanisms of action is likely to expand our knowledge of regulation at transcriptional and posttranscriptional levels in th eukaryotic cell. Several viral genes (*vif*, *vpu*, and **vpr**) facilit virus infection and/or release and may play a role in target cell and infection in vivo. The functions of yet other viral genes (ne remain unclear. Recent data also suggest that the *tat* gene produc have a role in **HIV** pathogenesis that goes beyond trans-activating expression. It can potentially impact on uninfected cells as a di molecule and alter the growth of different cell types.

L28 ANSWER 28 OF 55 MEDLINE on STN
91306450. PubMed ID: 1830183. Expression of **human immunodeficienc virus** type 1 *vif* and **vpr** mRNAs is Rev-dependent and regulated by splicing. Schwartz S; Felber B K; Pavlakis G N. (Human Retrovirus National Cancer Institute-Frederick Cancer Research and Developmen Center, Maryland 21702-1201.) Virology, (1991 Aug) 183 (2) 677-8 Journal code: 0110674. ISSN: 0042-6822. Pub. country: United State Language: English.

AB We have analyzed the structure and expression of the **HIV-1** *vif* an mRNAs. The results revealed that the predominant *vif* and **vpr** mRN belong to the intermediate size class of **HIV-1** mRNAs and that the expression is dependent on the presence of Rev protein. In additi levels of a small multiply spliced **vpr** mRNA were produced by **HIV**-cDNA cloning and expression of **vpr** cDNAs in eucaryotic cells revea that high levels of **Vpr** were produced only from the intermediate-mRNA in the presence of Rev. Thus, as demonstrated for the viral structural proteins, expression of *Vif* and **Vpr** is regulated by Re arrangement of the splice sites and the Rev-RRE interaction are responsible for the regulation of viral expression, and especially switching from an early stage, producing only or primarily *Tat*, *Re* *Nef* from multiply spliced mRNAs, to a late stage, leading to the production of *Gag*, *Pol*, *Env*, *Vpu*, *Vif*, and **Vpr** from unspliced and partially spliced mRNAs.

L28 ANSWER 29 OF 55 MEDLINE on STN
91302806. PubMed ID: 1712812. HLA-binding regions of **HIV-1** protei A systematic study of viral proteins. Choppin J; Martinon F; Conna Pauchard M; Gomard E; Levy J P. (Institut Cochin de Genetique Mole (ICGM), INSERM U152, Paris, France.) Journal of immunology (Balti Md. : 1950), (1991 Jul 15) 147 (2) 575-83. Journal code: 2985117R ISSN: 0022-1767. Pub. country: United States. Language: English.

AB To detect HLA-binding peptides in 10 **HIV-1** proteins (Rev, Tat, **Vpr**, Vpu, Gag p18, Gag p24, Gag p15, Env gp120 and Env gp41), the peptide binding assay (PBA) has been performed using three HLA class II molecules. Correlations have been searched between the PBA result and the peptide competitor activity in a functional test using HLA-A2-restricted CTL and target cells. A correlation between the results found in the PBA and well-defined CTL epitopes could be attempted for the three Gag proteins. For these proteins, our results are in agreement with the known existence of epitopes reacting with human CD8+ CTL, with some exceptions. Together with the results reported with a panel of peptides, these experiments showed that at least 18/20 of the already reported CTL epitopes from **HIV-1** Gag, Nef, and Env proteins could be detected by the PBA, most (17/18) corresponding to strong reactivity. Perhaps more important, the regions of **HIV-1** Gag p24 or Nef protein that contain multiple associated CTL epitopes, with different HLA restrictions, were clearly identified by the reactivities in the PBA. Several overlapping peptides and the major practical interest of this might be the detection of such polyepitopic regions. Prediction is proposed in this report for 10 proteins, including several proteins for which CTL epitopes remain presently unknown.

L28 ANSWER 30 OF 55 MEDLINE on STN
91293462. PubMed ID: 1829694. Molecular biology of the **human immunodeficiency virus** type 1. Haseltine W A. (Dana-Faber Cancer Institute, Harvard Medical School, Boston, Massachusetts 02115.) journal : official publication of the Federation of American Societies for Experimental Biology, (1991 Jul) 5 (10) 2349-60. Ref: 120. Journal code: 8804484. ISSN: 0892-6638. Pub. country: United States. Language: English.

AB The immunodeficiency virus type 1 is a complex retrovirus. In addition to the genes that specify the proteins of the virus particle and the reverse transcriptase and integrase common to all retroviruses, **HIV-1** specifies at least six additional proteins that regulate the virus life cycle. Two of these regulatory genes, tat and rev, specify proteins essential for reverse transcription. These proteins bind to specific sequences of newly synthesized viral RNA and profoundly affect virus protein expression. Tat and rev appear to be prototypes of novel eukaryotic regulatory proteins. These two genes play a central role in regulating the rate of virus replication. Other viral genes, vif, vpr, and **vpr**, affect the assembly and replication capacity of newly made virus particles. These genes may play a critical role in spread of the virus from tissue to tissue and from person to person. Our understanding of the contribution of each of these virus structural proteins and regulatory genes to the complex life cycle of the virus in natural infections is incomplete. However, enough has been gained into the structure and function of each of these components to provide a firm basis for rational antiviral drug development.

L28 ANSWER 31 OF 55 MEDLINE on STN
91291498. PubMed ID: 1829617. Formation of noninfectious **HIV-1** virions

particles lacking a full-length envelope protein. Ratner L; Vander N; Garcia J; Polinsky M; Westervelt P; Becich M. (Department of Me Washington University, St. Louis, MO 63110.) AIDS research and hu retroviruses, (1991 Mar) 7 (3) 287-94. Journal code: 8709376. ISS 0889-2229. Pub. country: United States. Language: English.

AB Deletions were constructed within a functional **human immunodeficiency virus type 1 (HIV-1)** proviral clone in order to assess the role of envelope protein in virus particle formation. A graded exonucleas deletion technique was used to produce 12 clones with deletions of nucleotides in the first conserved domain of envelope. This inclu clones with frameshift deletions and 3 clones with in-frame deletions. Isogenic pairs of env deletion clones were produced with or without additional deletion in the vif and **vpr** genes. Upon transfection, clones produced virus particles, as determined by p24 antigen, reverse transcriptase, and sucrose gradient assays with conditioned media. Particles produced from clones with deletions in env or vif and **vpr** both regions, banded on sucrose gradients with a mobility similar to virus produced by the parental clone. The p24 gag capsid protein of the particles was resistant to trypsin, but the particles were disrupted by treatment with Triton X-100, suggesting the presence of a surrounding lipid bilayer. Furthermore, electron microscopic studies revealed mature and immature virus particles derived from COS cells transfected with the env deletion clones. Cocultivation experiments with lymphocytes and cells transfected with each of the env deletion clones demonstrated that the virus particles were noninfectious.

L28 ANSWER 32 OF 55 MEDLINE on STN

91251200. PubMed ID: 2041078. Generation of a chimeric human and simian immunodeficiency virus infectious to monkey peripheral blood mononuclear cells. Shibata R; Kawamura M; Sakai H; Hayami M; Ishimoto A; Adachi M (Department of Viral Oncology, Kyoto University, Japan.) Journal of virology, (1991 Jul) 65 (7) 3514-20. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB We constructed five chimeric clones between **human immunodeficiency virus type 1 (HIV-1)** and simian immunodeficiency virus (SIVMAC) and four SIVMAC mutants by recombinant DNA techniques. Three chimeric clones and all mutants with an alteration in either the vif, vpx, **vpr**, or nef gene were infectious to human CD4-positive cell lines. The susceptibility of macaque monkey peripheral blood mononuclear cells (PBMC) to infection by these mutants and chimeras was examined in vitro. Macaque PBMC supported the replication of wild-type and vpx, **vpr**, and nef mutant SIVMAC strains. A chimera carrying the long terminal repeats (LTR) of SIVMAC and tat, rev, vpu, and env of HIV-1 was replication competent in PBMC. In contrast, HIV-1, the vif mutant SIVMAC, a chimera containing rev and env of SIVMAC, and a chimera containing vpx, **vpr**, tat, rev, and env of SIVMAC did not grow in PBMC. Western immunoblotting analysis of the replicating chimera in PBMC confirmed the hybrid nature of the virus. These data strongly suggest that the sequence important for macaque cell tropism lies within the gag, pol, and/or vif sequences of the SIVMAC genome.

L28 ANSWER 33 OF 55 MEDLINE on STN

91237814. PubMed ID: 1674547. Characterization of multiple mRNA sp
simian immunodeficiency virus from macaques in a CD4+ lymphoid cel
Park I W; Steen R; Li Y. (New England Regional Primate Research Ce
Harvard Medical School, Southborough, Massachusetts 01772.) Journ
virology, (1991 Jun) 65 (6) 2987-92. Journal code: 0113724. ISSN:
0022-538X. Pub. country: United States. Language: English.

AB Cytoplasmic poly(A)+ RNA was isolated from CEMX721.174 cells 5 to
after infection with molecularly cloned simian immunodeficiency vi
SIVmac239. Expression of SIV RNA was analyzed by Northern (RNA) b
hybridization and by sequencing of cDNA clones. As expected, a sp
donor site was demonstrated in the untranslated leader sequence ou
the left long terminal repeat. The region between pol and env was
to contain at least two splice donor and six splice acceptor sites
Splice acceptor and donor sites in the intergenic region were suit
positioned for expression of vpx, **vpr**, tat, and rev. Splice accep
sites at nucleotides 8802 and 8805 were demonstrated in singly and
spliced RNAs with the potential of expressing nef and the second e
tat and rev. Our results demonstrate a complex pattern of alterna
splicing of SIV mRNAs. The results are very similar to what has b
observed in **human immunodeficiency virus** type 1-infected cells,
suggesting that both human and simian immunodeficiency viruses are
to multiple levels of regulation.

L28 ANSWER 34 OF 55 MEDLINE on STN

91224490. PubMed ID: 1827422. Rev is necessary for translation but
cytoplasmic accumulation of **HIV-1** vif, **vpr**, and env/vpu 2 RNAs. A
S J; Chen I S. (Department of Microbiology, University of Californ
Angeles School of Medicine.) Genes & development, (1991 May) 5 (
808-19. Journal code: 8711660. ISSN: 0890-9369. Pub. country: Un
States. Language: English.

AB The effect of Rev on cytoplasmic accumulation of the singly splice
human immunodeficiency virus type 1 (**HIV-1**) vif, **vpr**, and
env/vpu RNAs was examined by using a quantitative RNA polymerase c
reaction (PCR) analysis following transfection of complete provira
molecular clones into lymphoid cells. Previously published studie
subgenomic env constructs in nonlymphoid cell types concluded that
necessary for cytoplasmic accumulation of high levels of unspliced
and that, by analogy, Rev must be necessary for the cytoplasmic
accumulation of all **HIV-1** RNAs that contain the Rev-responsive el
(RRE). We confirm those results in COS cells. Unexpectedly, in 1
cells, we find that although Rev acts somewhat to increase the cyt
level of full-length **HIV-1** RNA, Rev has little or no effect on
cytoplasmic accumulation of singly spliced **HIV-1** RNAs. However,
protein expression was greatly reduced in the absence of Rev. Ana
the cytoplasmic RNA revealed that in the absence of Rev or the RRE
cytoplasmic vif, **vpr**, and env/vpu 2 RNAs were not associated with
polysomes but with a complex of 40S-80S in size. Consequently, ef
expression of the Vif, **Vpr**, Vpu, and Env proteins from these RNAs

dependent on Rev. These results exclude a mechanism whereby the function of Rev is simply to export RNAs from nucleus to cytoplasm discuss other models to take into account the dependence on Rev for efficient translation of cytoplasmic **HIV-1** RNAs.

L28 ANSWER 35 OF 55 MEDLINE on STN

91205767. PubMed ID: 2017879. A defective proviral DNA with a 2.6 deletion of **human immunodeficiency virus** type 1 (**HIV-1**) in a persistently **HIV-1** infected cell clone. Imai H; Maotani-Imai K; S S; Ikuta K; Suehiro S; Kurimura T; Kato S; Hirai K. (Section of Se Hokkaido University, Sapporo, Japan.) *Virus genes*, (1991 Jan) 5 81-8. Journal code: 8803967. ISSN: 0920-8569. Pub. country: United States. Language: English.

AB A cell line (H2-5) producing defective doughnut-shaped particles **human immunodeficiency virus** type I (**HIV-1**) was found to contain proviral DNA with a large deletion of 2558 bases, corresponding to half of pol gene, the vif and **vpr** genes, and the 5' terminal of the gene.

L28 ANSWER 36 OF 55 MEDLINE on STN

91175192. PubMed ID: 2150318. **Human immunodeficiency virus vpr** gene encodes a virion-associated protein. Yuan X; Matsuda Z; Matsu Essex M; Lee T H. (Department of Cancer Biology, Harvard University of Public Health, Boston, MA 02115.) *AIDS research and human retroviruses*, (1990 Nov) 6 (11) 1265-71. Journal code: 8709376. I 0889-2229. Pub. country: United States. Language: English.

AB The **vpr** gene of **human immunodeficiency virus** type 1 (**HIV-1**) is one of the seven accessory genes that are believed to have roles in virus replication cycle. We report here the detection of a 13 kD protein in sucrose gradient-purified **HIV-1**. This protein was not detected in cells infected with a virus having a truncated **vpr** gene lacks the potential to encode for 26 C-terminal amino acid residues. These findings raise the possibility that virion-associated **vpr** protein may be involved in the early life cycle of **HIV-1** replication and that the C-terminal region of the **vpr** gene is essential for its expression.

L28 ANSWER 37 OF 55 MEDLINE on STN

91174658. PubMed ID: 1706590. Generation and characterization of **human immunodeficiency virus** type 1 mutants. Adachi A; Ono N; Saka H; Ogawa K; Shibata R; Kiyomasu T; Masuike H; Ueda S. (Institute for Research, Kyoto University, Japan.) *Archives of virology*, (1991) (1-2) 45-58. Journal code: 7506870. ISSN: 0304-8608. Pub. country: Austria. Language: English.

AB Mutations were introduced by recombinant DNA techniques into 9 genetically infectious molecular clones of **human immunodeficiency virus** type 1. The 24 mutants generated were characterized biochemically and biologically by transfection and infection experiments. None of the mutants with mutations in gag (p17, p24, and p15 regions), pol (protease, reverse transcriptase, and endonuclease domains), env (gp120 region), tat,

were infectious, whereas vif, **vpr**, vpu, some of env (gp41) and nef mutants could grow in human CD4+ cells to various degrees. Of the non-infectious mutants, only endonuclease (pol) and gp41 mutants e normal phenotypes with respect to the production of functional rev transcriptase, the expression of gag, pol, and env proteins, and t generation of progeny virions, when examined in transient assays. infectious mutants killed the CD4+ cells with the exception of a m carrying a defect in the vif gene.

L28 ANSWER 38 OF 55 MEDLINE on STN

91143122. PubMed ID: 2149621. Identification and localization of gene product of **human immunodeficiency virus** type 1. Sato A; Igarashi H; Adachi A; Hayami M. (Shionogi Institute for Medical Sc Osaka, Japan.) Virus genes, (1990 Dec) 4 (4) 303-12. Journal co 8803967. ISSN: 0920-8569. Pub. country: United States. Language: E

AB The entire **vpr** gene of **human immunodeficiency virus** type 1 (**HIV-1**) was cloned into procaryotic and eucaryotic expression vect Production of authentic protein encoded by the gene in bacterial a mammalian cells was monitored by Western blotting using guinea pig antisera raised against an N-terminal 14-oligopeptide of the pred **vpr** protein. A specific 12-kD protein was clearly detected with t antisera, but not with preimmune sera, in both cell systems, and t binding was blocked by the oligopeptide. These antisera also reco protein of the same size in several human T-cell lines infected w **HIV-1**. Western blotting analysis of subcellular fractions prepare the cells producing wildtype **vpr** protein strongly suggested that t protein was membrane associated. A region within the **vpr** require the stable expression of **vpr** product was also suggested by mutatio analyses.

L28 ANSWER 39 OF 55 MEDLINE on STN

91140768. PubMed ID: 1825343. Rev activates expression of the **hum immunodeficiency virus** type 1 vif and **vpr** gene products. Garrett D; Tiley L S; Cullen B R. (Howard Hughes Medical Institute, Duke University Medical Center, Durham, North Carolina 27710.) Journal virology, (1991 Mar) 65 (3) 1653-7. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The proteins encoded by **human immunodeficiency virus** type 1 (**HIV-1**) can be divided into two temporally regulated classes. Ear gene products are encoded by multiply spliced mRNA species and are expressed constitutively. In contrast, late proteins are encoded class of unspliced or singly spliced viral transcripts whose cytop expression is induced by the viral Rev trans activator. Here, we demonstrate that the viral Vif and **Vpr** proteins are encoded by sin spliced viral mRNAs whose expression is activated by Rev. This ac is shown to result from the reduced utilization of splice sites ad to or within the vif and **vpr** coding sequences. Vif and **Vpr** there belong to the class of late **HIV-1** gene products.

L28 ANSWER 40 OF 55 MEDLINE on STN

91122920. PubMed ID: 2149126. A synthetic protein corresponding to entire **vpr** gene product from the **human immunodeficiency virus HIV-1** is recognized by antibodies from **HIV**-infected patients. Gras-Masse H; Ameisen J C; Boutillon C; Gesquiere J C; Vian S; Ney L; Drobecq H; Capron A; Tartar A. (Biomolecular Chemistry Facility CNRS-1309, Pasteur Institute, Lille, France.) International journal peptide and protein research, (1990 Sep) 36 (3) 219-26. Journal 0330420. ISSN: 0367-8377. Pub. country: Denmark. Language: English

AB The 95 amino acid-protein encoded by the non-structural **vpr** gene **human immunodeficiency virus** type 1 (LAV-1BRU isolate) was chemically synthesized by solid phase methodology. The synthetic protein was characterized by amino acid analysis, sequence analysis, RP-HPLC, and urea-SDS PAGE. Using a radioimmunoassay, antibodies to synthetic protein were detected in sera of 25% of **HIV** 1-seropositive patients tested. Western blot analysis suggested that the antibodies preferentially recognize the dimeric form of **vpr**.

L28 ANSWER 41 OF 55 MEDLINE on STN

91090981. PubMed ID: 2265025. Nucleotide sequence of a Ugandan **HI** provirus reveals genetic diversity from other **HIV-1** isolates. Ora Downing R G; Roff M; Clegg J C; Serwadda D; Carswell J W. (Division Pathology, PHLS Centre for Applied Microbiology and Research, Salisbury, England.) AIDS research and human retroviruses, (1990 Sep) 6 (9) 1073-8. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB A Ugandan isolate of **human immunodeficiency virus** type 1 (**HIV-1**), designated U455, was adapted to growth in U937 cells, the provirus integrated into the lambda L47.1 vector, and its DNA sequence determined. The sequences of some of the U455 genes showed a marked divergence from those of North American and other African isolates. The sequenced clone was defective with single in-phase stop codons in the **vpr** and **env** genes, resulting in a stop codon, within the **vpu** gene.

L28 ANSWER 42 OF 55 MEDLINE on STN

91045941. PubMed ID: 2236020. The **human immunodeficiency virus** type 2 **vpr** gene is essential for productive infection of human macrophages. Hattori N; Michaels F; Fargnoli K; Marcon L; Gallo R C; Franchini A. (Laboratory of Tumor Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.) Proceedings of the National Academy of Sciences of the United States of America, (1990 Oct) 87 (10) 8080-4. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The **human immunodeficiency virus** (**HIV**) genetic determinant(s) responsible for tropism in human T cells or macrophages are not well defined. We studied the role of the **HIV** type 2 (**HIV-2**) **nef** and **v** genes in viral tropism. **HIV-2** mutants, lacking either **vpr** or **nef** genes, or both **vpr** and **nef**, were obtained by site-specific mutagenesis of a biologically active **HIV-2** proviral clone (**HIV-2sbl/isy**), which was infectious in both human T cells and macrophages. Viral progeny containing mutations of **nef**, **vpr**, or of both **nef** and **vpr** genes replicated more

efficiently than the parental virus in primary human peripheral blood cells and in the human Hut 78 T-cell line. In contrast, the **HIV-**mutant infected human macrophages as efficiently as the parental virus whereas viruses lacking the **vpr** gene either alone or in conjunction with the lack of the **nef** gene did not replicate in macrophages. Thus, lack of **nef** in **HIV-2** enhances viral replication in T cells and does not interfere with viral replication in primary macrophages, whereas **nef** is essential for replication of **HIV-2** in human macrophages. Because parental **HIV-2** also infects rhesus macaques, these studies of these **HIV-2** mutants with differences in cell tropism and rates of replication will be highly useful in understanding the mechanism of viral infectivity and possibly pathogenicity in vivo.

L28 ANSWER 43 OF 55 MEDLINE on STN

91039259. PubMed ID: 2231682. Mutational analysis of simian immunodeficiency virus from African green monkeys and **human immunodeficiency virus** type 2. Shibata R; Adachi A; Sakai H; Ishimura A; Miura T; Hayami M. (Institute for Virus Research, Kyoto University, Japan.) Journal of medical primatology, (1990) 19 (3-4) 217-25. Journal code: 0320626. ISSN: 0047-2565. Pub. country: Denmark. Language: English.

AB We constructed ten mutants of simian immunodeficiency virus isolate from African green monkey (SIVAGM), and nine mutants of **human immunodeficiency virus** type 2 (**HIV-2**) in vitro. Their infectivity, cytopathogenicity, transactivation potential, virus RNA, and protein synthesis were examined by transfection and infection experiments. Mutations in three structural (**gag**, **pol**, **env**) and two regulatory (**tat**, **rev**) genes abolished the infectivity of both viruses, but **vpx**, **vpr** (**HIV-2**) and **nef** were dispensable and mutant viruses were indistinguishable phenotypically from wild type virus. A **vif** mutant of **HIV-2** showed infectivity in cell-free condition, whereas SIVAGM mutants grew equally well with wild type virus. In transient transfection assays, **rev** derived from both viruses produced mainly small mRNA species and no detectable virus proteins and particles. Transactivation potential of mutants originated from both viruses was about three- to ten-fold higher than that of respective wild type DNAs, generating small amounts of

L28 ANSWER 44 OF 55 MEDLINE on STN

90347862. PubMed ID: 2384924. Characterization and expression of a singly spliced RNA species of **human immunodeficiency virus** type 1. Arrigo SJ; Weitsman S; Zack JA; Chen IS. (Department of Microbiology and Immunology, UCLA School of Medicine.) Journal of virology, (Sep) 64 (9) 4585-8. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB **Human immunodeficiency virus** type 1 (**HIV-1**) expresses the **Vif**, **Vpr**, **Vpu**, and **Env** proteins through complex differential splicing of a single full-length RNA precursor. We used **HIV-1**-specific oligonucleotide primer pairs in a quantitative polymerase chain reaction procedure on RNA from fresh peripheral blood lymphocytes infected with **HIV-1** to detect and characterize the singly spliced RNA species.

which might encode these proteins. The nucleotide sequences at the junctions of splice donor and acceptor sites of these RNAs were determined. One of these RNAs, which has not been previously described appears to be a novel **HIV-1** RNA encoding Env and/or Vpu proteins.

L28 ANSWER 45 OF 55 MEDLINE on STN

90320150. PubMed ID: 2371777. The env gene variability is not directly related to the high cytopathogenicity of an HIV1 variant. Spire B; I; Neuveut C; Sire J; Chermann J C. (Unité de Recherches INSERM sur le Retrovirus et Maladies Associées U322, Campus Universitaire de Luminy Marseille, France.) *Virology*, (1990 Aug) 177 (2) 756-8. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB HIV1-NDK is a Zairian HIV1 isolate which is unique because of its cytopathic effect on T lymphoblastoid cell lines. Its sequence analysis has indicated 30% divergence with HIV1-LAV/BRU HTLVIII B prototype env gene encoding for the envelope glycoprotein gp120. In order to correlate the highly cytopathic properties with the env genetic variability, recombinants between the HIV1 prototype and HIV1-NDK have been constructed, including HIV1-NDK env gene, and their cytopathic phenotypes were analyzed. The viral hybrid containing all HIV1 protein sequences except a large fragment including the total HIV1-NDK envelope remained at a low cytopathic phenotype. Our results suggest that sequences other than the env gene namely p18 gag, vif, and **vpr** are required for the high virulence of HIV1-NDK.

L28 ANSWER 46 OF 55 MEDLINE on STN

90257596. PubMed ID: 2341832. Speed of progression to AIDS and delayed antibody response to accessory gene products of **HIV-1**. Reiss P; L M; de Ronde A; de Wolf F; Dekker J; Debouck C; Goudsmit J. (Department of Virology, University of Amsterdam, the Netherlands.) *Journal of medical virology*, (1990 Mar) 30 (3) 163-8. Journal code: 7705876. ISSN: 0146-6615. Pub. country: United States. Language: English.

AB Antibodies to E. coli-produced **HIV-1** nef, rev, tat, vpu, and **vpr** proteins were measured by enzyme immunoassay in serial sets of sera from 72 men seroconverting for antibodies to **HIV-1** structural proteins from 190 initially symptom-free men who were seropositive for these antibodies at entry into the study. In the men seroconverting for antibodies to structural proteins the levels of nef-, rev-, and tat-specific antibodies, but not of vpu-, and **vpr**-specific antibodies within 3 months of seroconversion, appeared to be lower in the men progressing to AIDS, compared with the men remaining symptom-free at follow-up. Analysis of the prevalence of previously described antibody profiles to these accessory gene products was carried out. In all antibody seroconverters and in those **HIV-1** antibody seropositive with 15 or more months of follow-up who progressed to AIDS, there was a shift from predominantly nef- and vpu-specific antibody negative profiles in the men developing AIDS in the early years of the study to predominantly nef- and vpu-specific antibody positive profiles in developed AIDS later. Rev- and tat-specific antibody negative profiles were dominant in men progressing to AIDS throughout follow-up. N

vpr-specific antibody profile occurred preferentially in the men progressing to AIDS throughout follow-up. Low antibody reactivity accessory gene products **nef**, **rev**, and **tat** appears, like low anti-antibody reactivity, to be associated with progression to AIDS rel rapidly after infection with **HIV-1**.

L28 ANSWER 47 OF 55 MEDLINE on STN

90244434. PubMed ID: 2139896. **Human immunodeficiency virus vpr** product is a virion-associated regulatory protein. Cohen E A; Dehn Sodroski J G; Haseltine W A. (Division of Human Retrovirology, Dan Cancer Institute, Boston, Massachusetts.) Journal of virology, (**Jun**) 64 (6) 3097-9. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The **vpr** product of the **human immunodeficiency virus** type 1 (**HIV-1**) acts in trans to accelerate virus replication and cytopath effect in T cells. Here it is shown that the **HIV-1** viral particl contains multiple copies of the **vpr** protein. The **vpr** product is first regulatory protein of **HIV-1** to be found in the virus particl This observation raises the possibility that **vpr** acts to facilita early steps of infection before de novo viral protein synthesis oc

L28 ANSWER 48 OF 55 MEDLINE on STN

90112644. PubMed ID: 2296082. Mutational analysis of the **human immunodeficiency virus** type 2 (**HIV-2**) genome in relation to **HIV-1** and simian immunodeficiency virus SIV (AGM). Shibata R; Miura T; H Ogawa K; Sakai H; Kiyomasu T; Ishimoto A; Adachi A. (Department of Oncology, Kyoto University, Japan.) Journal of virology, (**1990 F** (2) 742-7. Journal code: 0113724. ISSN: 0022-538X. Pub. country: States. Language: English.

AB We constructed an infectious molecular clone of the **human immunodeficiency virus** type 2 (**HIV-2**) and generated nine frameshift mutants corresponding to nine open reading frames identified so fa Three structural (**gag**, **pol**, **env**) and two regulative (**tat**, **rev**) gen mutants were not infectious, whereas **vif**, **vpx**, **vpr**, and **nef** genes dispensable for infectivity. All of the mutants except **env** and re cytopathic in CD4+ human leukemia cells. In transfection assays, expression of **HIV-2** long terminal repeat was activated by infectio clones of **HIV-1**, **HIV-2**, and simian immunodeficiency virus from Afr green monkey but not by the **tat** mutants. However, an **HIV-2** **tat** m could produce small amounts of virus proteins and particles in con a **rev** mutant, which directed no detectable synthesis of virus prot virions.

L28 ANSWER 49 OF 55 MEDLINE on STN

90112005. PubMed ID: 2136912. Antibody response to viral proteins and R (**vpr**) in **HIV-1**-infected individuals. Reiss P; Lange J M; de Ronde A; de Wolf F; Dekker J; Danner S A; Debouck C; Goudsmit J. (Department of Virology, University of Amsterdam, The Netherlands. Journal of acquired immune deficiency syndromes, (**1990**) 3 (2) 115 Journal code: 8812597. ISSN: 0894-9255. Pub. country: United State

Language: English.

AB Antibodies to E. coli-produced **HIV-1 vpr** and vpu were determined by enzyme immunoassay in serial sets of sera from 72 men seroconverting antibodies to **HIV-1** structural proteins, and from 196 initially symptom-free men who were positive for such antibodies at study entry. First detection of **vpr**- and vpu-specific antibodies always was within months of seroconversion for antibodies to structural proteins. In a combined cohort of 268 men, **vpr**- and vpu-specific antibodies were persistently in 26 and 43% of men, respectively. **Vpr**- and vpu-specific antibodies were transiently detected in 3 and 7%, respectively, and intermittently detected in 18 and 13% of men, respectively. No association was found between the patterns of **vpr**- or vpu-specific antibody response and clinical outcome. In subjects with different patterns of **vpr**- and vpu-specific antibody response, no clear temporal relationship existed between the appearance or disappearance of an antibody and the onset of **HIV-1**-related disease.

L28 ANSWER 50 OF 55 MEDLINE on STN

90079752. PubMed ID: 2136707. Identification of **HIV-1 vpr** product function. Cohen E A; Terwilliger E F; Jalilovs Y; Proulx J; Sodroski J; Haseltine W A. (Department of Human Retrovirology, Dana-Farber Cancer Institute, Harvard Medical School, Massachusetts 02115.) Journal of acquired immune deficiency syndromes, (1990) 3 (1) 11-8. Journal ISSN: 0894-9255. Pub. country: United States. Language: English.

AB To investigate the role of **vpr** (viral protein R) in the replication and cytopathicity of human immunodeficiency virus type 1 (**HIV-1**), infectious proviruses were constructed that were isogenic except for the ability to produce the protein product of **vpr**. The experiments described here demonstrate that **vpr** encodes a 96 amino acid 15 kDa protein. The **vpr** product increases the rate of replication and accelerates the cytopathic effect of the virus in T cells. **Vpr** also transactivates to increase levels of viral protein expression. The stimulatory effect of **vpr** is observed to act on the **HIV-1** LTR as well as on several heterologous promoters.

L28 ANSWER 51 OF 55 MEDLINE on STN

90074393. PubMed ID: 2590553. Serum reactivity to **HIV-1** accessory products distinguishes East African from West African **HIV** strains infecting agent. Goudsmit J; Dekker J T; Boucher C A; Smit L; De Rubeck C; Barin F. (Human Retrovirus Laboratory, Academic Medical Center, Amsterdam, The Netherlands.) AIDS research and human retroviruses (Oct) 5 (5) 475-7. Journal code: 8709376. ISSN: 0889-2229. Report No.: PIP-060605; POP-00193107. Pub. country: United States. Language: English.

AB The existence of dual infections with human immunodeficiency virus type 1 (**HIV-1**) and 2 in West African countries has been controversial, although the current consensus is that dual infection is not the cause of the extensive cross-reactivity observed between these 2 viruses. To evaluate the role of antibody reactivity to the **HIV-1** accessory gene products, type-specific **HIV** serology, proteins encoded for nef, tat, rev, v

and vpu were developed and used as an antigen. 5 of the 7 exclusiv **HIV-2** reactive sera were not reactive to the **HIV-1** accessory gene products. Moreover, the 2 sera that showed reactivity to the **HIV** envelope were the only ones reactive to **HIV-1** accessory gene prod These findings indicate that type 2 viruses may be as diverse as t viruses. A subsequent analysis of sera from 24 West Africans reve reactivity with a simian immunodeficiency virus (SIV) peptide but an **HIV-1** peptide previously shown to be discriminatory in a direct binding assay between **HIV-1** and **HIV-2**. Compared to 29 control ser from East Africans, the West Africa sera had significantly lower reactivity to antibodies specific to nef, tat, and rev; there was reactivity to **vpr** and vpu. 38% of the West African sera compared w 93% of the East African sera showed reactivity to **HIV-1** accessory products. It is concluded that, while reactivity to the **HIV-1** ac gene products **vpr** and vpu indicate **HIV-1** infection, reactivity to other accessory gene products cannot be used to identify virus typ the documented cross-reactivity to **HIV-1** accessory gene products o antibodies elicited by **HIV-2** strains.

L28 ANSWER 52 OF 55 MEDLINE on STN

89342662. PubMed ID: 2474678. Mutational analysis of the **human immunodeficiency virus vpr** open reading frame. Ogawa K; Shibata R; Kiyomasu T; Higuchi I; Kishida Y; Ishimoto A; Adachi A. (Departmen Viral Oncology, Kyoto University, Japan.) Journal of virology, (**Sep**) 63 (9) 4110-4. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Mutations were introduced by recombinant DNA techniques into the open reading frame of an infectious molecular clone of **human immunodeficiency virus** type 1. The effect of these changes on the replicative and cytopathologic properties of the virus recovered f transfected cells was studied in several human CD4+ lymphocyte cel In all cases, mutant viruses were infectious and cytopathic. Howe when a low-input dose was used, mutants grew significantly more sl than the wild-type virus. The growth kinetics of **vpr** mutants wer distinct from those of vif and vpu mutants.

L28 ANSWER 53 OF 55 MEDLINE on STN

89259383. PubMed ID: 2724559. Isolation of **HIV-2** from AIDS patien Ghana and analysis of sero-reactive patterns of Ghanaian sera. Hay Nippon rinsho. Japanese journal of clinical medicine, (1989 Jan) 141-8. Journal code: 0420546. ISSN: 0047-1852. Report No.: PIP-061100; POP-00203853. Pub. country: Japan. Languag Japanese.

AB Institute for Virus Research, Kyoto University, and Noguchi Memori Research Institute in Ghana jointly isolated **HIV-2** from a Ghanaia patient. Ghanaian **HIV-2**[GH-1] was similar in genomic organization but different in Restriction Enzyme Maps from the first isolated c French LAV-2 (**HIV-2**ROD). This fact is significant in suggesting multiplicity of **HIV-2** virus. **HIV-2**[GH-1] was different from LAV- its antigenicity of envProtein. Sero-reactive patterns of 125 Gha

including 57 AIDS/ARC patients were analyzed using HIV-1, HIV-2, SIVAGM as antigen. 4 groups were recognized. Group I was HIV-1 o positive; Group II, HIV-2-only positive; Group III, mixed HIV-1 a HIV-2 positive; Group IV reacted to gag protein of HIV-1, HIV-2 a SIVAGM but not to envProtein of any. 24 Ghanians were HIV-1 posit were HIV-2 positive. 19 out of 20 HIV-2-only positive patients wer AIDS/ARC patients. Symptoms and route of infection from HIV-1 an HIV-2 AIDS seem to be similar but HIV-2 is weaker pathologically a in communicability. HIV positive patients were mostly found in th city such as Accra among young women, especially prostitutes who w migratory "workers" in neighboring countries along the Ivory Coast Sero-reactive patterns of Ghanaians with SIV as antigen had been k some time to be different from those of Kenyans in the east coast those of Gabonese. While KEnyan's antibody was high for HIV-1 an for SIVAGM, Ghanian's was higher for SIVAGM than HIV-1. Gabonese in between. With discovery of LAV-2 (HIV-2ROD) and Ghanian hybridization with its DNA probe Ghanaian's was found to have amon things VPX and VPR in common with HIV-2ROD.

L28 ANSWER 54 OF 55 MEDLINE on STN
89259122. PubMed ID: 2524599. **Viral protein R of human immunodeficiency virus** types 1 and 2 is dispensable for replicatio and cytopathogenicity in lymphoid cells. Dederá D; Hu W; Vander He Ratner L. (Department of Medicine, Washington University, St. Loui Missouri 63110.) Journal of virology, (1989 Jul) 63 (7) 3205-8. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United State Language: English.

AB **Viral protein R (VPR)** is conserved in **human immunodeficiency virus** types 1 and 2 (HIV-1 and HIV-2). To assess its function, we have constructed mutations within the **vpr** coding regions of HIV-1 HIV-2 predicted to express truncated **VPR** products. Infectious vir was produced by each proviral clone and showed similar replication kinetics and cytopathogenicity when compared with the correspondin parental proviral clone.

L28 ANSWER 55 OF 55 MEDLINE on STN
89089998. PubMed ID: 2850118. **Animal models for HIV infection and memorandum from a WHO meeting.** Anonymous. Bulletin of the World He Organization, (1988) 66 (5) 561-74. Journal code: 7507052. ISSN: 0042-9686. Report No.: PIP-054632; POP-00186454. Pub. country: Switzerland. L English.

AB The **human immunodeficiency virus** is a member of the lentivirus subfamily of the retrovirus family. Retroviruses are RNA viruses code for an RNA-dependent DNA polymerase (reverse transcriptase), transcribes the RNA genome into a DNA provirus which, on integrati the host DNA, directs the synthesis of new virions. The RNA genom consists of a gag gene, which codes for the viral core proteins, a gene, which codes for the reverse transcriptase, an env gene, whic for the glycoproteins of the viral envelope, and several genes (ta

vif, **vpr**, and nef), that code for regulatory proteins. At each end of the genome are long terminal repeats, that contain regulatory elements for transcription. There are 3 subfamilies of Retroviridae (Oncovirinae, Spumavirinae, and Lentivirinae). The Lentivirinae ("slow viruses") include the bovine immunodeficiency virus (BIV), the feline immunodeficiency virus (FIV), the human immunodeficiency viruses (HIV) and the simian immunodeficiency viruses (SIV). SIV has been isolated from macaques (mac), African green monkeys (agm), sooty mangabeys (sm), mandrills (mnd). Only SIVmac causes an AIDS-like disease in its host, but it is genetically closer to **HIV-2** than to **HIV-1**. SIVsm causes an AIDS-like disease in macaques, but not in the sooty mangabeys. Monkeys infected with SIV develop diarrhea, wasting, decrease in T lymphocytes, lymphadenopathy, development of giant cells, and encephalitis, as well as opportunistic infections. Kaposi's sarcoma, however, has not been found in SIV-infected primates. Virus is recovered from peripheral blood mononuclear cells and the brain. SIV models are useful for understanding the natural history of primate lentivirus, defining the pathogenesis of AIDS, and for developing vaccines. The SIV model would be one in which **HIV** causes AIDS, but so far only chimpanzees and gibbons have successfully been infected with **HIV-1**, and although the virus is recovered from peripheral blood mononuclear cells of chimpanzees within 2 weeks of infection, and 2 animals have lost antibodies to the virus, none has so far developed clinical AIDS. Attempts to develop vaccines to immunize chimpanzees are continuing. Nonprimate lentiviruses include the visna virus, the feline immunodeficiency virus, and the equine immunodeficiency virus. The visna virus infects fibroblasts by fusion of the viral envelope with the plasma membrane of the fibroblast; it infects macrophages by endocytosis. Infected macrophages regulate the production and dissemination of viral particles. The feline immunodeficiency virus infects T-lymphocytes of cats and produces oral, gastrointestinal and respiratory pathology as well as lymphadenopathy and opportunistic infections. Bovine immunodeficiency-like virus causes a generalized lymphadenopathy similar to that seen in AIDS-related complex.

=> d 128,cbib,ab,1-24

L28 ANSWER 1 OF 55 MEDLINE on STN

94047336. PubMed ID: 8230445. Incorporation of **Vpr** into human immunodeficiency virus type 1 virions: requirement for the p6 region of gag and mutational analysis. Paxton W; Connor R I; Landau N R. Diamond AIDS Research Center, New York, New York.) Journal of virology (1993 Dec) 67 (12) 7229-37. Journal code: 0113724. ISSN: 0022-5387. Pub. country: United States. Language: English.

AB The product of the **vpr** open reading frame of human immunodeficiency virus type 1 (**HIV-1**) is a 15-kDa, arginine-rich protein that is present in virions in molar quantities equivalent to that of Gag. We report here the results of our investigations into the mechanism by which **Vpr** is incorporated into virions during assembly in infected cells. In these studies we used an expression vector encoding a **Vpr** molecule

at its amino terminus to a nine-amino-acid peptide from influenza hemagglutinin. The tagged **Vpr** expression vector and a **vpr** mutant **HIV-1** provirus were used to cotransfect COS cells, and the resulting virions were tested for the presence of the tagged protein on immunoprobed with monoclonal antibody against the hemagglutinin peptide. COS-produced virions were found to contain readily detectable amounts of tagged **Vpr** and smaller amounts of a putative tagged **Vpr** dimer. Infectivity of the particles was not altered by incorporation of the **Vpr**. Our results using this system in combination with mutant **HIV-1** proviruses suggested that incorporation of **Vpr** into virions requires the carboxy-terminal Gag protein of **HIV-1** (p6) but not gp160, Pol, or genomic viral RNA. In addition, analysis of mutated, tagged **Vpr** molecules suggested that amino acids near the carboxy terminus (amino acids 84 to 94) are required for incorporation of **Vpr** into **HIV-1** virions. The single cysteine residue near the carboxy terminus was required for production of a stable protein. Arginine residues were not important for incorporation or stability of tagged **Vpr**. These results suggested a novel strategy for blocking **HIV-1** replication.

L28 ANSWER 2 OF 55 MEDLINE on STN

94016888. PubMed ID: 8411397. Context-dependent role of **human immunodeficiency virus** type 1 auxiliary genes in the establishment of chronic virus producers. Mustafa F; Robinson H L. (Department of Medical Genetics, University of Massachusetts Medical Center, Worcester 01601) *Journal of virology*, (1993 Nov) 67 (11) 6909-15. Journal code: 0 ISSN: 0022-538X. Pub. country: United States. Language: English.

AB Two molecularly cloned viruses, **human immunodeficiency virus** type 1 (HIV-1)-NL4-3 (NL4-3) and HIV-1-HXB-2 (HXB-2), have been used to study the role of HIV-1 auxiliary genes in the establishment of chronic virus producers. NL4-3 encodes all known HIV-1 proteins, whereas HXB-2 is defective for three auxiliary genes: **vpr**, **vpu**, and **nef**. Studies were done in H9 cells, a T-cell line unusually permissive for the establishment of chronic virus producers. NL4-3 and HXB-2 undergo lytic phases of infection in H9 cultures with HXB-2, but not NL4-3, supporting the efficient establishment of chronic virus producers. Tests of mutant genomes containing various combinations of defective auxiliary genes revealed that both **vpr** and **nef** limited the ability of NL4-3 to establish chronic virus producers. Tests of a series of recombinants between NL4-3 and HXB-2 revealed that 5' internal sequences as well as fragments containing defective auxiliary genes affected the establishment of chronic virus producers. Viral envelope sequences and levels of virus production did not correlate with the ability to establish chronic virus producers. These results suggest that complex interactions of viral auxiliary and nonauxiliary gene functions with the host cell determine the ability to establish chronic virus producers.

L28 ANSWER 3 OF 55 MEDLINE on STN

94016837. PubMed ID: 8411357. **Human immunodeficiency virus** type 1 **viral protein R** localization in infected cells and virions. Lu Y L; Spearman P; Ratner L. (Department of Medicine, Washington University School of Medicine, St. Louis, MO 63110) *Journal of virology*, (1993 Nov) 67 (11) 6909-15. Journal code: 0 ISSN: 0022-538X. Pub. country: United States. Language: English.

School of Medicine, St. Louis, Missouri 63110.) Journal of virology (1993 Nov) 67 (11) 6542-50. Journal code: 0113724. ISSN: 0022-53 Pub. country: United States. Language: English.

AB The subcellular localization of **human immunodeficiency virus** type (HIV-1) **viral protein R (Vpr)** was examined by subcellular fractionation. In HIV-1-infected peripheral blood mononuclear cells **Vpr** was found in the nuclear and membrane fractions as well as the conditioned medium. Expression of **Vpr** without other HIV-1 proteins in two different eukaryotic expression systems, demonstrated a pre localization of **Vpr** in the nuclear matrix and chromatin extract fractions. Deletion of the carboxyl-terminal 19-amino-acid arginine sequence impaired **Vpr** nuclear localization. Indirect immunofluorescence confirmed the nuclear localization of **Vpr** and also indicated a perinuclear location. Expression of **Vpr** alone did not result in export of the protein from the cell, but when coexpressed with the Gag protein **Vpr** was exported and found in virus-like particles. A truncated Gag protein, missing the p6 sequence and a portion of the p9 sequence, incapable of exporting **Vpr** from the cell. Regulation of **Vpr** localization may be important in the influence of this protein on replication.

L28 ANSWER 4 OF 55 MEDLINE on STN

94016835. PubMed ID: 8411355. Analysis of simian immunodeficiency sequence variation in tissues of rhesus macaques with simian AIDS. T; Mori K; Kawahara T; Ringler D J; Desrosiers R C. (Division of Pathology, Oregon Regional Primate Research Center, Medical Research Foundation of Oregon, Beaverton 97006.) Journal of virology, (1993 Nov) 67 (11) 6522-34. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB One rhesus macaque displayed severe encephalomyelitis and another displayed severe enterocolitis following infection with molecularly cloned simian immunodeficiency virus (SIV) strain SIVmac239. Little or no anti-SIV antibody developed in these two macaques, and they died relatively quickly (4 to 6 months) after infection. Manifestation of tissue-specific disease in these macaques was associated with the emergence of variants with high replicative capacity for macrophage primary infection of tissue macrophages. The nature of sequence variation in the central region (vif, **vpr**, and **vpx**), the env gene, and the long terminal repeat (LTR) region in brain, colon, and other tissues was examined to see whether specific genetic changes were associated with replication in brain or gut. Sequence analysis revealed strong conservation of the intergenic central region, nef, and the LTR. Analysis of env sequences in these two macaques and one other revealed significant, interesting patterns of sequence variation. (i) Changes in env that were found previously to contribute to the replicative ability of SIVmac for macrophages in culture were present in the tissues of these animals. (ii) The greatest variability was located in the regions V1 and V2 and from "V3" through C3 in gp120, which are different from the variable regions observed previously in animals with strong antibody responses and long-term persistent infection. (iii)

predominant sequence change of D-->N at position 385 in C3 is most surprising, since this change in both SIV and **human immunodeficiency virus** type 1 has been associated with dramatically diminished affinity for CD4 and replication in vitro. (iv) The nature of sequence changes at some positions (146, 178, 345, 385, and "V3") suggests that viral replication in brain and gut may be facilitated by specific sequence changes in env in addition to those that impart a general ability to replicate well in macrophages. These results demonstrate that, under selective pressures, including immune responses and varying cell and tissue specificity, can influence the nature of sequence changes in

L28 ANSWER 5 OF 55 MEDLINE on STN

94016817. PubMed ID: 8411338. Alternative splicing of **human immunodeficiency virus** type 1 mRNA modulates viral protein expression, replication, and infectivity. Purcell D F; Martin M A. (Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892.) Journal of virology, (1993) (11) 6365-78. Journal code: 0113724. ISSN: 0022-538X. Pub. count United States. Language: English.

AB Multiple RNA splicing sites exist within **human immunodeficiency virus** type 1 (**HIV-1**) genomic RNA, and these sites enable the synthesis of many mRNAs for each of several viral proteins. We evaluated the biological significance of the alternatively spliced mRNA species produced in productive **HIV-1** infections of peripheral blood lymphocytes and human T-cell lines to determine the potential role of alternative RNA splicing in the regulation of **HIV-1** replication and infection. First, we used a semiquantitative polymerase chain reaction of cDNAs that were radiolabeled for gel analysis to determine the relative abundance of the diverse products of alternatively spliced **HIV-1** mRNAs. The predominant rev, tat, and env RNAs contained a minimum of noncoding sequence, but the predominant nef mRNAs were incompletely spliced and invariably included noncoding exons. Second, the effect of altered RNA processing was measured following mutagenesis of the major 5' splice donor and several cryptic, constitutive, and competing 3' splice acceptor motifs of **HIV-1** NL4-3. Mutations that ablated constitutive splice sites led to activation of new cryptic sites; some of these preserved biological function. Mutations that ablated competing splice acceptor sites marked alterations in the pool of virus-derived mRNAs and, in some instances, in virus infectivity and/or the profile of virus protein products. Redundant RNA splicing signals in the **HIV-1** genome and alternatively spliced mRNAs provides a mechanism for regulating the relative production of **HIV-1** proteins and, in some cases, viral infectivity.

L28 ANSWER 6 OF 55 MEDLINE on STN

93301098. PubMed ID: 8314984. Enzyme-linked oligosorbent assay for detection of polymerase chain reaction-amplified **human immunodeficiency virus** type 1. Mallet F; Hebrard C; Brand D; Chapuis E; Cros P; Allibert P; Besnier J M; Barin F; Mandrand B. (Unité de Microbiologie, Centre National de la Recherche Scientifique-bioMérieux, Ecole Normale Supérieure de Lyon, France.) Journal of clinical

microbiology, (1993 Jun) 31 (6) 1444-9. Journal code: 7505564. IS 0095-1137. Pub. country: United States. Language: English.

AB An enzyme-linked oligosorbent assay (ELOSA) was developed for the detection on microtiter plates of polymerase chain reaction (PCR)-amplified **human immunodeficiency virus** type 1 (**HIV-1**) DNA. The denatured PCR product was hybridized with a passively adsorbed oligonucleotide capture probe and a horseradish peroxidase-labeled oligonucleotide detection probe. The sensitivity and specificity of the PCR-ELOSA technique depended to some extent on the nucleotide sequence of the oligonucleotide primer and probe quartet used in the amplification and detection. We evaluated five oligonucleotide quartets located in the *pol*, *vpr*, *env*, and *nef* regions of **HIV-1**. DNAs from 39 **HIV-1**-seropositive individuals and 27 healthy **HIV-1**-seronegative controls were amplified by the PCR procedure, and the products were detected by ELOSA. Ten copies of **HIV-1** DNA against a background of 1 microgram of human DNA were specifically detected by PCR-ELOSA. Specificities and sensitivities were, respectively, 100 and 95% for the *gag* system, 100 and 97% for the *pol* system, 100 and 85% for the *v* system, 96 and 95% for the *env* system, and 100 and 95% for the *nef* system. The simplicity of ELOSA makes it suitable for automation and application in genetic testing and detection of viral and bacterial DNAs or RNAs in routine laboratories.

L28 ANSWER 7 OF 55 MEDLINE on STN

93287266. PubMed ID: 8510229. Antisense phosphorothioate oligodeoxynucleotides targeted to the *vpr* gene inhibit **human immunodeficiency virus** type 1 replication in primary human macrophages. Balotta C; Lusso P; Crowley R; Gallo R C; Franchini G (Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda, Maryland 20892.) Journal of virology, (1993 Jul) 67 (7) 4409-14. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The replication of human immunodeficiency viruses (**HIV**) in human macrophages is influenced by genetic determinants which have been predominantly related to the viral envelope. However, in **HIV-2**, the *vpr* gene has also been suggested as an important modulator of viral expression in human macrophages. We synthesized five antisense phosphorothioate oligodeoxynucleotides complementary to the *vpr* mRNA of **HIV-1Ba-L**, a highly macrophage-tropic viral strain, and measured their effect on **HIV-1Ba-L** replication in primary human macrophages. All of the oligodeoxynucleotides displayed some level of non-sequence-specific inhibition of viral replication; however, only the antisense one had an additional effect on viral production in primary macrophages. Of the antisense oligodeoxynucleotides tested, only one did not show any additional effect on viral production, whereas all the others inhibited viral replication to a similar degree (70 to 100%). Variation in the degree of inhibition was observed by using five different donors of primary macrophages. The phosphorothioate oligonucleotides, targeting the initiating methionine of the *Vpr* protein, had an inhibitory effect at both 20 and 10 microM only when the size was increased from 24

bases. Thus, **HIV-1** replication in human macrophages is modulated expression of the **vpr** gene, and it is conceivable that **vpr** antisense oligodeoxynucleotides could be used in combination with antisense oligodeoxynucleotides against other **HIV-1** regulatory genes to better control viral expression in human macrophages.

L28 ANSWER 8 OF 55 MEDLINE on STN

93216509. PubMed ID: 8463132. Persistently **human immunodeficiency virus** type 1-infected T cell clone expressing only doubly spliced exhibits reduced cell surface CD4 expression. Kishi M; Nishino Y; Kimura T; Ikuta K. (Section of Serology, Hokkaido University, Sappo Japanese journal of cancer research : Gann, (1993 Feb) 84 (2) 153 Journal code: 8509412. ISSN: 0910-5050. Pub. country: Japan. Language: English.

AB Several cell clones possessing the **human immunodeficiency virus** type 1 (**HIV-1**) genome, consisting of an almost full-length DNA sequence isolated by limiting dilution of the clonal cell line M10 derived from MT-4 that survived infection with **HIV-1 vpr** mutant (M10/**vpr**-). One of the isolated clones (termed **Vpr-1**) expressed only doubly spliced mRNA, but not unspliced or singly spliced mRNA. Western blots of total protein revealed the presence of the **nef** translation product, although no expression of major structural genes such as **gag**, **pol**, and **env** was detected by indirect immunofluorescence and assay of reverse transcriptase activity. These **HIV-1** phenotypes differed greatly from those of the original M10/**vpr**-, most of which expressed major structural **HIV-1** proteins. Despite undetectable levels of **env** expression in **Vpr-1**, **HIV-1** antigens were greatly down-modulated on the surface without alteration of steady-state levels of CD4 mRNA expression, similar to M10/**vpr**-. **HIV-1** phenotypes in **Vpr-1** did not change after the treatment of the cells with both phorbol 12-myristate 13-acetate and phytohemagglutinin. Therefore, the abnormal **HIV-1** life cycle in **Vpr-1** seems to be due to some viral factor(s), as well as cellular factors. Thus, **Vpr-1** could be a useful model for understanding one **HIV-1** latent form.

L28 ANSWER 9 OF 55 MEDLINE on STN

93177836. PubMed ID: 8440020. Induction of cell differentiation by **immunodeficiency virus** type 1 **vpr**. Levy D N; Fernandes L S; Williams W; Weiner D B. (Department of Medicine, University of Pennsylvania, Philadelphia.) Cell, (1993 Feb 26) 72 (4) 541-50. Journal code: 0413066. ISSN: 0092-8674. Pub. country: United States. Language: English.

AB Cell lines from rhabdomyosarcomas, which are tumors of muscle origin, have been used as models of CD4-independent **HIV** infection. These cell lines can be induced to differentiate in vitro. We report here that the **vpr** gene of **HIV-1** is sufficient for the differentiation of the human rhabdomyosarcoma cell line TE671. Differentiated cells are characterized by great enlargement, altered morphology, lack of replication, and low level expression of the muscle-specific protein myosin. We have also observed the morphological differentiation and inhibition of proliferation of two other transformed cell lines. **vpr**-transfected cells remain viable in culture for extended periods. These observations elucidate

potential role for **vpr** in the virus life cycle and raise the possibility that some aspects of **HIV**-induced pathologies may be caused by a disturbance of cells by **vpr**.

L28 ANSWER 10 OF 55 MEDLINE on STN

93174930. PubMed ID: 8438567. Intracellular transport and virion incorporation of vpx requires interaction with other virus type-s components. Kappes J C; Parkin J S; Conway J A; Kim J; Brouillette Shaw G M; Hahn B H. (Department of Medicine, University of Alabama Birmingham 35294.) *Virology*, (1993 Mar) 193 (1) 222-33. Journal 0110674. ISSN: 0042-6822. Pub. country: United States. Language: E

AB Viral protein X (vpx) is a virion-associated **HIV-2**/SIV accessory that enhances viral infectivity and replication in natural target. To investigate whether other viral components affect its biosynthesis, subcellular localization, and virion incorporation, we expressed vpx in a mammalian cell system and examined its transport and packaging requirements using an in trans complementation assay. The complete coding region of **HIV-2**ST was placed under the control of a high-efficiency promoter system (SR alpha) which contained both an promoter/enhancer region and R/U5 elements of the HTLV-1 LTR. Following transfection of Cos-1 cells, this construct (pSR alpha-vpx) facilitated high level expression of vpx, as demonstrated by Western blot analysis of transfected cell lysates. Moreover, indirect immunofluorescence analysis revealed an intense vpx staining pattern distributed evenly throughout cytoplasm of transfected cells. This distribution differed markedly from cells expressing wild-type **HIV-2** in which vpx localized to the inner surface of the plasma membrane. To determine whether other **HIV** components were required for this surface localization, we expressed vpx in the context of replication competent **HIV-1** and **HIV-2** proviruses. Following cotransfection with a vpx-deficient **HIV-2** provirus (pXM), vpx eukaryotically expressed vpx targeted to the plasma membrane and colocalized with **HIV-2** p27 gag in a pattern indistinguishable from wild-type **HIV-2**. Moreover, progeny virions from cotransfected Cos cells contained wild-type amounts of vpx protein, demonstrating that vpx could be efficiently packaged in trans. Under the same experimental conditions, cotransfection of vpx with wild-type **HIV-1** (pHXB2) or a **vpr**-deficient **HIV-1** (pR2) failed to result in detectable cell surface targeting or virion incorporation of vpx despite its high level of expression. These results demonstrate that efficient intracellular transport and packaging of vpx require interaction with other type-specific virus components.

L28 ANSWER 11 OF 55 MEDLINE on STN

93172371. PubMed ID: 8382307. A distinct African lentivirus from S monkeys. Hirsch V M; Dapolito G A; Goldstein S; McClure H; Emau P; N; Isahakia M; Lenroot R; Myers G; Johnson P R. (Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Rockville, Maryland 20852.) *Journal of virology*, (1993 Mar) 67 (1) 1517-28. Journal code: 0113724. ISSN: 0022-538X. Pub. country: U States. Language: English.

AB Asymptomatic infection with simian immunodeficiency virus (SIV) has demonstrated in African Sykes' monkeys (*Cercopithecus mitis albugo*) and virus isolation confirmed infection with a novel SIV from Sykes monkeys (SIVsyk). Macaques inoculated with SIVsyk became persistently infected but remained clinically healthy. We utilized polymerase chain reaction amplification to generate a full-length, infectious molecular clone of SIVsyk. The genome organization of SIVsyk is similar to the other primate lentiviruses, consisting of gag, pol, vif, vpr, rev, env, and nef. A unique feature is the absence of the highly conserved NF-kappa B binding site in the long terminal repeat. SIVsyk is genetically equidistant from other primate lentiviruses. Thus, SIVsyk represents a new group that is distinct from the four previously recognized primate lentivirus groups: **human immunodeficiency virus type 1 (HIV-1)**, SIV from sooty mangabeys (SIVsmm) and **HIV-2**, SIV from African green monkeys (SIVagm), and SIV from mandrills (SIVmdr). Genetic differences between SIVsyk and SIVagm, isolates derived from monkeys of the same genus, underscore the potential for other distinct SIVs which have yet to be isolated and characterized.

L28 ANSWER 12 OF 55 MEDLINE on STN
93172330. PubMed ID: 8437208. Integration is essential for efficient expression of **human immunodeficiency virus type 1**. Sakai H; Kawamura M; Sakuragi J; Sakuragi S; Shibata R; Ishimoto A; Ono N; Ueda S; Aizawa T (Institute for Virus Research, Kyoto University, Japan.) Journal of virology, (1993 Mar) 67 (3) 1169-74. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB A mutant of **human immunodeficiency virus type 1** which carries a frameshift insertion in the integrase/endonuclease region of pol constructed in vitro. Upon transfection into cells, although this mutant exhibited a normal phenotype with respect to expression of gag, pol, and env genes and to generation of progeny virions, no replication-competent virus in CD4-positive cells emerged. An assay for the single-step replication of a defective viral genome dependent on trans complementation by rev protein was established and used to monitor the early phase of viral infection process. Viral clones with a mutation in the vif, or vpr gene displayed no abnormality in the early phase. In contrast, the integrase mutant did not direct a marker gene expression after infection. Together with an observation that the mutant lacked the ability to integrate, these results indicated that the integration was required for efficient viral gene expression and productive infection of **human immunodeficiency virus type 1**.

L28 ANSWER 13 OF 55 MEDLINE on STN
93021387. PubMed ID: 1404605. Complete nucleotide sequence, genome organization, and biological properties of **human immunodeficiency virus type 1** in vivo: evidence for limited defectiveness and complementation. Li Y; Hui H; Burgess C J; Price R W; Sharp P M; Hahn B H; Shaw G M. (Department of Medicine, University of Alabama, Birmingham 35294-0007.) Journal of virology, (1992 Nov) 66 (11) 6587-600. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

English.

AB Previous studies of the genetic and biologic characteristics of **human immunodeficiency virus** type 1 (**HIV-1**) have by necessity used tissue culture-derived virus. We recently reported the molecular cloning of full-length **HIV-1** genomes directly from uncultured human brain tissue (Y. Li, J. C. Kappes, J. A. Conway, R. W. Price, G. M. Shieh, B. H. Hahn, J. Virol. 65:3973-3985, 1991). In this report, we describe the biologic properties of these four clones and the complete nucleotide sequences and genome organization of two of them. Clones **HIV-1YU-1** and **HIV-1YU-10** were 9,174 and 9,176 nucleotides in length, differed by 10 nucleotides in nucleotide sequence, and except for a frameshift mutation in the *env* gene in **HIV-1YU-10**, contained open reading frames corresponding to 5'-gag-pol-vif-vpr-tat-rev-vpu-env-nef-3' flanked by long terminal repeats. **HIV-1YU-2** was fully replication competent, while **HIV-1YU-1** and two other clones, **HIV-1YU-21** and **HIV-1YU-32**, were defective. The three defective clones, however, when transfected into Cos-1 cell lines in pairwise combination, yielded virions that were replication competent and transmissible by cell-free passage. The cellular host range of **HIV-1YU-2** was strictly limited to primary T lymphocytes and monocyte-macrophages, a property conferred by its external envelope glycoprotein. Phylogenetic analyses of **HIV-1YU-2** gene sequences revealed this virus to be a member of the North American/European subgroup, with specific similarity to other monocyte-tropic virus V3 envelope amino acid sequence. These results indicate that **HIV** infection of brain is characterized by the persistence of mixtures of fully competent, minimally defective, and more substantially altered forms and that complementation among them is readily attainable. In addition, the limited degree of genotypic heterogeneity observed among **HIV-1YU** and other brain-derived viruses and their preferential tropism for monocyte-macrophages suggest that viral replication within the nervous system may differ from that within the peripheral lymphoid compartment in significant and clinically important ways. The availability of genetically and biologically well characterized **HIV** clones from uncultured human tissue should facilitate future studies of virus-cell interactions relevant to viral pathogenesis and drug and vaccine development.

L28 ANSWER 14 OF 55 MEDLINE on STN
92410594. PubMed ID: 1529528. Cell-free transmission of Vif mutant **HIV-1**. Fan L; Peden K. (Laboratory of Molecular Microbiology, NIAI, NIH, Bethesda, Maryland 20892.) Virology, (1992 Sep) 190 (1) 19-24. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB To determine the phenotype of **human immunodeficiency virus** type 1 (**HIV-1**) defective in the production of Vif, mutations were introduced into the *vif* gene of infectious molecular clones of the LAI, MAL, and HTLV strains. Previous results had demonstrated that viruses derived from these wild type clones display different replicative capacities on peripheral blood mononuclear cells (PBMC) and different tropisms for CD4-positive cell lines. Using cell-free infection, Vif mutants of

MAL, and ELI were found to have delayed kinetics and to produce less than their corresponding wild type viruses when propagated on most permissive cell lines. An additional mutation in the **vpr** gene in LAI strain had no effect on this phenotype. However, on one T cell the H9 cell line, two Vif mutants of LAI and a Vif.Vpr double mutant were unable to replicate. Furthermore, Vif mutants from all three were only able to establish a productive infection on PBMC by coculture and not by cell-free infection. No defects in the processing of viral proteins or the release of particles in the Vif mutants were detected.

L28 ANSWER 15 OF 55 MEDLINE on STN

92371448. PubMed ID: 1324171. Evolution of the primate lentivirus evidence from vpx and **vpr**. Tristem M; Marshall C; Karpas A; Hill F (Department of Haematology, University of Cambridge Clinical School EMBO journal, (1992 Sep) 11 (9) 3405-12. Journal code: 8208664. I 0261-4189. Pub. country: ENGLAND: United Kingdom. Language: English

AB The genomes of the four primate lentiviral groups are complex and several regulatory or accessory genes. Two of these genes, **vpr** and **vpx** are found in various combinations within the four groups and encode proteins whose functions have yet to be elucidated. Comparison of encoded protein sequences suggests that the vpx gene within the H group arose by the duplication of an ancestral **vpr** gene within the group. Evolutionary distance analysis showed that both genes were conserved when compared with viral regulatory genes, and indicated the duplication occurred at approximately the same time as the HI group and the other primate lentivirus groups diverged from a common ancestor. Furthermore, although the SIVagm vpx proteins are homologous to the HIV-2 group vpx proteins, there are insufficient grounds from sequence analysis for classifying them as vpx proteins. Because of similarity to the **vpr** proteins of other groups, we suggest reclassify the SIVagm vpx gene as a **vpr** gene. This creates a simpler and more uniform picture of the genomic organization of the primate lentiviruses and allows the genomic organization of their common precursor to be defined; it probably contained five accessory genes: tat, rev, vif and **vpr**.

L28 ANSWER 16 OF 55 MEDLINE on STN

92365147. PubMed ID: 1501290. Effect of reciprocal complementation defective human immunodeficiency virus type 1 (HIV-1) molecular clones on HIV-1 cell tropism and virulence. Lori F; Hall L; Lusso Popovic M; Markham P; Franchini G; Reitz M S Jr. (Laboratory of Tumor Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.) Journal of virology, (1992 Sep) 66 (9) 5553-60. Journal code: 0113724. ISSN: 0022-538X. Pub. country: U States. Language: English.

AB Human immunodeficiency virus type 1 (HIV-1) displays both interstrain and intrastrain genetic variability. Virus population with extensive microheterogeneity have been defined as swarms or quasispecies. Many of the genomes within HIV-1 swarms appear to be defective in

more genes required for viral replication. It is unclear to what defective viruses play a role in the process of **HIV-1** infection of the pathogenesis of AIDS. We have isolated two biologically active **HIV-1** clones: LW 12.3, which contains defects in the *vif* and *vpr* genes, and MN ST.1, which has a defect in the *vpu* gene. LW 12.3 is able to replicate in peripheral blood mononuclear cells (PBMC). The growth of MN-ST.1 in SupT1 cells is marked by a 3-week lag in extracellular production and by the presence of unusually abundant viral buds. We demonstrate here that coinfection of PBMC with these two partially defective **HIV-1** clones extends the cellular host range of LW 12.3, significantly increases the replication rate of both viral genomes, and eliminates the delay in production observed with the *vpu*-defective ST.1. When the lesions in *vpr* and *vif* of LW 12.3 are repaired, the resultant virus grows normally in PBMC. This is also the case when *vif* is repaired, indicating that complementation of LW 12.3 in PBMC by ST.1 is mediated by *vif* in trans. The reciprocal complementation results in a dramatic increase of **HIV-1** virulence. This two-component model represents a simplified version of the in vivo situation and illustrates one way in which interaction of defective viruses could increase the spread of infection and progression of disease.

L28 ANSWER 17 OF 55 MEDLINE on STN

92309177. PubMed ID: 1613662. Infection of cynomolgus monkeys with chimeric **HIV-1**/SIVmac virus that expresses the **HIV-1** envelope glycoproteins. Li J; Lord C I; Haseltine W; Letvin N L; Sodroski J (Department of Pathology, Harvard Medical School, Boston, Massachusetts) Journal of acquired immune deficiency syndromes, (1992) 5 (7) 639. Journal code: 8812597. ISSN: 0894-9255. Pub. country: United States. Language: English.

AB Replication competent chimeric viruses that express the *gag* and *pol* proteins of SIVmac and the *env* proteins of **HIV-1** were made. One chimeric virus, SHIV-4, that expresses the *vif*, *vpx*, *vpr*, and *nef* regulatory genes of SIV and the *tat* and *rev* regulatory genes of **HIV-1** replicated efficiently in cynomolgus monkeys. This model system was used to evaluate the efficacy of anti-**HIV-1** vaccines directed at envelope glycoproteins, anti-**HIV-1** envelope glycoprotein antiserum, monoclonal antibodies, and anti-**HIV-1** drugs designed to inhibit the *rev*, or *env* functions.

L28 ANSWER 18 OF 55 MEDLINE on STN

92260672. PubMed ID: 1533883. Dual regulation of silent and productive infection in monocytes by distinct **human immunodeficiency virus type 1** determinants. Westervelt P; Henkel T; Trowbridge D B; Orenstein J; Heuser J; Gendelman H E; Ratner L. (Department of Medicine, Washington University School of Medicine, St. Louis, Missouri 63110.) Journal of virology, (1992 Jun) 66 (6) 3925-31. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The regulation of **human immunodeficiency virus type 1** infection and its replication in primary monocytes was investigated by mutagenesis of recombinant proviral clones containing an *env* determinant required

infectivity of monocytes. Virus replication was assayed by determination of reverse transcriptase activity in culture fluids and by recovery of virus from monocytes following cocultivation with uninfected peripheral blood mononuclear cells. Three virus replication phenotypes were observed in monocytes: productive infection, silent infection, and no infection. Incorporation of the monocyctotropic env determinant in a full-length virus incapable of infection or replication in primary monocytes (no infection) conferred the capacity for highly efficient virus replication in monocytes (productive infection). Clones with the env determinant but lacking either functional **vpr** or **vpu** genes generated lower replication levels in monocytes. Mutation of both **vpr** and **vpu**, however, resulted in near complete attenuation of virus replication in monocytes, despite successful virus recovery from infected monocytes by cocultivation with uninfected peripheral blood mononuclear cells (silent infection). These findings indicate a central role for the "accessory" genes **vpu** and **vpr** in productive **human immunodeficiency virus** type 1 replication in monocytes and indicate that **vpu** and **vpr** may be capable of function complementation.

L28 ANSWER 19 OF 55 MEDLINE on STN
92239218. PubMed ID: 1571200. **HIV** with multiple gene deletions as attenuated vaccine for AIDS. Desrosiers R C. (New England Regional Research Center, Harvard Medical School, Southborough, MA 01772-9 AIDS research and human retroviruses, (1992 Mar) 8 (3) 411-21. R Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States Language: English.

AB Most viral vaccines currently in use in humans are live attenuated viruses that lack pathogenic potential. In general, such live attenuated vaccines induce the strongest longest-lasting immunity. Live attenuated strains of **human immunodeficiency virus** type 1 (**HIV-1**) have not been previously considered as vaccines for acquired immunodeficiency syndrome (AIDS) because of an inability to envision how their safety could be adequately assured. This report describes a means for making live nonpathogenic strains of **SIVmac** and **HIV-1** that cannot revert to a virulent form and a stepwise scheme for demonstrating their safety. Replication-competent, multiply deleted derivatives that are currently being tested are missing combinations of auxiliary genes (**nef**, **vpv**, **vpx**, **vpu**) and certain control elements in the negative regulatory region (NRE) of the long terminal repeat (LTR). Since these genomic regions are in large part conserved among the **SIVs** and **HIVs**, they are likely to be important for the virus life cycle in vivo. Consistent with this reasoning, a replication-competent **nef** deletion mutant of **SIVmac** apparently has lost most or all of its pathogenic potential, yet it induces strong immune responses. Multiply deleted derivatives of **SIVmac** and **HIV-1** will have to be extensively tested in animal models prior to moving a promising **HIV-1** candidate to initial trials in high-risk volunteers. Definitive evidence for safety and general acceptance of this approach can only evolve gradually over a prolonged period of

L28 ANSWER 20 OF 55 MEDLINE on STN

92239216. PubMed ID: 1571198. Genetic and biological comparisons of pathogenic and nonpathogenic molecular clones of simian immunodeficiency virus (SIVmac). Luciw P A; Shaw K E; Unger R E; Planelles V; Stout Lackner J E; Pratt-Lowe E; Leung N J; Banapour B; Marthas M L. (Department of Medical Pathology, University of California, Davis 95616.) AIDS research and human retroviruses, (1992 Mar) 8 (3) 395-402. Ref: Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States Language: English.

AB Simian immunodeficiency virus (SIV) is a designation for a group of related but unique lentiviruses identified in several primate species. A viral isolate from a rhesus macaque (i.e., SIVmac) causes a fatal AIDS-like disease in experimentally infected macaques, and several infectious molecular clones of this virus have been characterized. This report presents the complete nucleotide sequence of molecularly cloned SIVmac1A11, and comparisons are made with the sequence of molecularly cloned SIVmac239. SIVmac1A11 has delayed replication kinetics in T cells but replicates as well as uncloned SIVmac in macrophage cultures. Macaques infected with virus from the SIVmac1A11 clone develop antibodies, but virus does not persist in peripheral blood mononuclear cells and no disease signs are observed. SIVmac239 infects lymphocytes, shows restricted replication in cultured macrophages, and establishes a persistent infection in animals that leads to a fatal AIDS-like disease. Both viruses are about 98% homologous at the nucleotide sequence level. In SIVmac1A11, the *vpr* gene as well as a transmembrane domain of *env* are prematurely truncated, whereas the *env* gene of SIVmac239 is prematurely truncated. Sequence differences noted in variable region 1 (V1) in the surface domain of the *env* gene are discussed with respect to the phenotypes of both viruses. This model is critically important for investigating the roles of specific viral genes in viral/host interactions that cannot be studied in individuals infected with the human immunodeficiency virus (HIV).

L28 ANSWER 21 OF 55 MEDLINE on STN

92233680. PubMed ID: 1568359. [Acquired immunodeficiency virus (HIV). Biological aspects and virological diagnosis]. Il virus dell'immunodeficienza acquisita (HIV-1). Aspetti biologici e diagnostici virologici. Dianzani F; Antonelli G; Turriziani O; Riva E. (Istituto di Virologia, Università degli Studi di Roma La Sapienza.) La Clinica terapeutica, (1992 Feb) 140 (2) 179-86. Ref: 20. Journal code: 03 ISSN: 0009-9074. Pub. country: Italy. Language: Italian.

AB The etiologic agent of the acquired immunodeficiency syndrome is a retrovirus included in the subclass of lentiviruses in view of characteristics common to these viruses. Their similarity is mainly represented by the extreme slowness of disease manifestation and by the fact that HIV, like other lentiviruses, spreads within the organism in spite of an immune reaction. The mechanism of replication is not dissimilar to that of other retroviruses except for the expression of a particularly large number of regulating genes the most important of which are called *tat*, *rev*, and *nef*. Further genes with a probable regulatory function are also present.

function are nef, **vpr**, and vpx. In the field of diagnostic virology together with normal isolation tests, a technique that has become particularly important is PCR (polymerase chain reaction) which allows to obtain a relevant amount of specific viral DNA sequences by the use of DNA polymerase and specific primers.

L28 ANSWER 22 OF 55 MEDLINE on STN

92198222. PubMed ID: 1550494. Biological characterization of **human immunodeficiency virus** type 1 and type 2 mutants in human peripheral blood mononuclear cells. Akari H; Sakuragi J; Takebe Y; Tomonaga K; Kawamura M; Fukasawa M; Miura T; Shinjo T; Hayami M. (Research Center for Immunodeficiency, Kyoto University, Japan.) Archives of virology, (1992) 123 (1-2) 157-67. Journal code: 7506870. ISSN: 0304-8608. country: Austria. Language: English.

AB Mutants of **human immunodeficiency virus** type 1 (HIV-1) and type 2 (HIV-2), which have been shown to be infectious in established cell lines, were tested for ability to replicate and induce syncytium formation in human peripheral blood mononuclear cells (PBMC). The vpx mutant HIV-1 showed depressed kinetics of replication in an established T cell line, as reported previously, but in PBMC, its replication was similar to that of the wild type virus. The vpx gene of HIV-2 was required for efficient virus propagation in PBMC, but not in an established T cell line, as previously reported. However, the growth rates of the virus in PBMC preparations from two individuals were different. The results of experiments on infection of PBMC with the vif and **vpr** mutants of HIV-1 and HIV-2 were essentially consistent with previous results of infection of established T cell lines. No negative effect of the nef gene product of HIV-1 and HIV-2 was observed. The abilities of the wild type virus and the mutants of HIV-1 to induce syncytium formation in both PBMC established cell lines were similar. In contrast, neither the wild type nor any of the mutants of HIV-2 induced syncytium formation in PBMC. These results suggest that the functions of some genes can be determined only in mixed populations or primary cells such as PBMC. Studies on the roles of these genes in PBMC may provide a better understanding of their functions in vivo.

L28 ANSWER 23 OF 55 MEDLINE on STN

92113582. PubMed ID: 1730943. Cells surviving infection by **human immunodeficiency virus** type 1: vif or vpx mutants produce non-infectious or markedly less cytopathic viruses. Kishi M; Nishi Sumiya M; Ohki K; Kimura T; Goto T; Nakai M; Kakinuma M; Ikuta K. (Institute of Immunological Science, Hokkaido University, Sapporo, Japan.) Journal of general virology, (1992 Jan) 73 (Pt 1) 77-87. Journal code: 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Under conditions in which a clonal cell line (M10) isolated from a cell lymphotropic virus type I-transformed MT-4 cell line was completely killed by infection with wild-type **human immunodeficiency virus** type 1 (HIV-1), equivalent M10 cells survived infection with HIV-1 vif **vpr** or vpx mutant virus after transient cytopathic effects. Severe

cell clones, which were isolated from the proliferating M10 cells infection with vif and vpu mutant viruses (M10/vif- and M10/vpu-) heterogeneous **HIV-1** phenotypes in terms of **HIV-1** antigen expression, their syncytium forming capacity, reverse transcriptase activity and infectivity of **HIV-1** particles produced. When the replication kinetics of the **HIV-1** particles produced were assayed in M10 cells, the clones could be classified into three types, i.e. type I producing non-infectious **HIV-1**, type II producing infectious **HIV-1** with low replicative ability and type III producing infectious **HIV-1** with a replicative ability similar to that of wild-type **HIV-1**. **HIV-1** major viral cell proteins and virus particle fractions were almost typical in types II and III but not in type I. Electron microscopic examination of particles released from type I, II and III clones revealed rare defective, predominantly defective and essentially normal virions, respectively. Northern and Southern blot analyses revealed no apparent deletion in the proviral DNA and mRNA prepared from these clones, except in the case of type I and II clones isolated from M10/vpu- which contained large deletions in the mRNA gag and gag-pol proteins. Thus, M10 cells surviving infection with **HIV-1** vif or vpu mutants are heterogeneous, persistently expressing **HIV-1** antigens and producing non-infectious or less cytopathic viruses.

L28 ANSWER 24 OF 55 MEDLINE on STN

92085377. PubMed ID: 1727477. Distinct RNA sequences in the gag region of **human immunodeficiency virus** type 1 decrease RNA stability and inhibit expression in the absence of Rev protein. Schwartz S; Felb P; Pavlakis G N. (Human Retrovirus Section, National Cancer Institute-Frederick Cancer Research and Development Center, Maryland 21702-1201.) Journal of virology, (1992 Jan) 66 (1) 150-9. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The expression of Gag, Pol, Vif, Vpr, Vpu, and Env proteins from unspliced and partially spliced **human immunodeficiency virus** type 1 (HIV-1) mRNAs depends on the viral protein Rev, while the production of Tat, Rev, and Nef from multiply spliced mRNAs does not require Rev. To investigate the difference between gag and tat mRNAs, we generated plasmids expressing tat-gag hybrid mRNAs. Insertion of the gag gene downstream of the tat open reading frame in the tat cDNA resulted in inhibition of Tat production. This inhibition was caused, at least in part, by a decrease in the stability of the produced mRNA. Deletion of a 218-nucleotide inhibitory sequence named INS-1 and located at the 5' end of the gag gene. Further experiments indicated the presence of more than one inhibitory sequence in the gag-protease gene region of the viral genome. The inhibitory effect of INS-1 was counteracted by the positive effect mediated by the Rev-Rev-responsive element interaction, indicating that this sequence is important for Rev-regulated gag expression. The INS-1 sequence did not contain any known HIV-1 splice sites and acted independently of splicing. It was found to have an unusually high AU content (61.5% AU), a common feature among cellular mRNAs with short half-lives. These results suggest that HIV-1 and possibly other lentiviruses have evolved to express unstable mRNAs.

require additional regulatory factors for their expression. This may offer the virus several advantages, including the ability to e state of low or latent expression in the host.

=> d his

(FILE 'HOME' ENTERED AT 07:59:12 ON 04 APR 2005)

FILE 'USPATFULL' ENTERED AT 07:59:21 ON 04 APR 2005

```
L1          1 S US4808536/PN
L2          1 S US5001230/PN
L3          1 S US5874225/PN
            E WEINER DAVID B/IN
L4          57 S E1 OR E3
L5          33 S L4 AND (VPR OR VIRAL PROTEIN R)
L6          33 S L5 AND (ANTIBOD?)
L7          19 S L6 AND (ANTIBOD? (8W) VPR) OR (ANTIBOD? (8W) VIRAL PR
L8          18 S L7 AND (ANTIBOD?/CLM OR VPR/CLM OR VIRAL PROTEIN R/CL
L9          38258 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L10         728 S L9 AND (VPR OR VIRAL PROTEIN R)
L11         675 S L10 AND ANTIBOD?
L12         21 S L11 AND AY<1994
L13        141 S L10 AND (VPR/CLM OR VIRAL PROTEIN R/CLM)
L14         40 S L13 AND ANTIBOD?/CLM
L15         2 S L14 AND AY<1994
L16         6 S L13 AND AY<1994
L17         4 S L16 NOT L15
```

FILE 'WPIDS' ENTERED AT 08:20:18 ON 04 APR 2005

```
            E WEINER DAVID B/IN
            E WEINER D B/IN
L18         66 S E3
L19         10 S L18 AND (VPR OR VIRAL PROTEIN R)
L20        189 S (VPR OR VIRAL PROTEIN R)
L21         0 S L20 AND (VPR/AB OR VIRAL PROTEIN R/AB)
L22        32 S L20 AND AY<1994
L23        30 S L22 NOT L19
```

FILE 'USPATFULL' ENTERED AT 08:27:37 ON 04 APR 2005

```
L24         1 S US6706268/PN
```

FILE 'MEDLINE' ENTERED AT 08:29:34 ON 04 APR 2005

```
L25        150879 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L26        677 S L25 AND (VPR OR VIRAL PROTEIN R)
L27        606 S L26 AND (VPR/AB OR VIRAL PROTEIN R/AB)
L28        55 S L27 AND PY<1994
```

=> log off

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:y

STN INTERNATIONAL LOGOFF AT 08:42:17 ON 04 APR 2005